The Journal
OF THE KANSAS MEDICAL SOCIETY

Sixth Annual University of Kansas

School of Medicine Number

COMPLETE TABLE OF CONTENTS . . . Page IV

March 1952 Vol. LII, No. 3

STORMONT MEDICAL LIBRARY
TOPEKA, KANSAS
MAR 20 1952

ONE FLUIDOUNCE
SOLUTION
ADRENALIN
CHLORIDE
(P. D. & CO.
1:1000 'ADRENALIN'
For Topical Application
Each fluidounce contains 'ADRENALIN' (Epinephrine, P. D. & Co.) 9/20 grain as the hydrochloride, dissolved in physiological salt solution.
STOCK NO. 22-3-26
PARKE, DAVIS & CO.
DETROIT, MICH., U. S. A.

Adrenalin®

(epinephrine, Parke-Davis)

the first

hormone to be isolated in pure crystalline form

the first

American antihistaminic

Benadryl® HYDROCHLORIDE

(diphenhydramine hydrochloride, Parke-Davis)

Theelin

(ketohydroxyestratriene, Parke-Davis)

the first

crystalline estrogenic substance

Chloromycetin®

(chloramphenicol, Parke-Davis)

the first

and only antibiotic synthesized on a practical scale

The Parke-Davis label, known and relied on the world over, is a respected symbol in research, in clinical investigation, and in quality production.

Parke, Davis & Company

DETROIT, MICHIGAN

TABLE OF CONTENTS

MARCH, 1952

ORIGINAL ARTICLES

A Working Program for the Care and Treatment of the Hypertensive Patient—E. Grey Dimond, M.D., Kansas City, Kansas 105

Surgical Injuries of the Urinary Tract—Raymond W. Stockton, M.D., and Robert H. Owens, M.D., Kansas City, Kansas 107

Harelip and Cleft Palate: Modern Trends in Management—David W. Robinson, M.D., Kansas City, Kansas 114

Terminal Bronchiolar or "Alveolar Cell" Carcinoma of Lung: A Case Report—H. H. Dunham, M.D., and V. G. Smith, M.D., Kansas City, Kansas 117

Two Attacks of Endocarditis Caused by Different Microorganisms—Joe L. Stockard, M.D., Kansas City, Kansas 122

Intravenous Avertin: A Preliminary Report—Roger W. Bumgarner, M.D., Richard L. Pokorny, M.D., Ernst T. Morch, M.D., and Paul H. Lorhan, M.D., Kansas City, Kansas 124

A Method for the Rectal Use of Nisulfazole in Chronic Ulcerative Colitis—William R. Durkee, M.D., Manhattan, Kansas 127

Hemorrhagic Transfusion Reactions—Charles H. McCroskey, M.D., and Stanley R. Friesen, M.D., Kansas City, Kansas 129

EDITORIALS

Sixth Annual University Issue 133

Kansas Medical Day 133

American Medical Education Fund 134

Annual Meeting, April 27-May 1 134

Entered as second-class matter, May 2, 1914, at the Postoffice at Topeka, Kansas, under the Act of March 3, 1879. Accepted for mailing at special rate of postage provided for in Section 1103, October 3, 1917. Authorized on July 2, 1918.

THE JOURNAL OF THE KANSAS MEDICAL SOCIETY

EDITORIAL BOARD

LUCIEN R. PYLE, M.D., Editor, Topeka

ORVILLE R. CLARK, M.D., Topeka
JOHN W. CAVANAUGH, M.D., Topeka
DWIGHT LAWSON, M.D., Topeka
RICHARD GREER, M.D., Topeka

ASSOCIATE EDITORS

DONALD P. TREES, M.D., Wichita
GLEN R. SHEPHERD, M.D., Kansas City

INFORMATION

Ownership: The Journal is a non-profit publication owned and published monthly by The Kansas Medical Society.

Subscription: Membership in The Kansas Medical Society includes subscription to The Journal. Rates to others, except in foreign countries, are $4.00 per year or 60c per copy.

Material: Scientific articles, editorials, and data of general interest are invited from all members. Articles are to be submitted on condition that they are contributed solely to this publication. A right is reserved to reject any material deemed unsatisfactory.

Manuscripts: Only manuscripts that are typewritten on one side, double spaced, and original copies can be accepted. Manuscripts will be returned upon request.

Advertising: All advertising contracts, and all copy from advertisers under contract are subject to approval of the editorial board. Copy should be received by the 20th of the month immediately preceding the month of publication.

Reprints: Actual cost prices for reprints will be quoted upon request. Reprints should be ordered promptly after publication or forms may not be available.

Non-Responsibility: Although an effort is made to publish only accurate articles and legitimate advertisements the Journal denies legal responsibility for any statements, opinions, or advertisements appearing under the names of contributors or concerns.

PAULINE FARRELL, Managing Editor and Advertising Manager

OLIVER E. EBEL, Business Manager

Publication Office: 512 New England Building, Topeka

Cortone®

Can be used Safely in the Prolonged Control of Rheumatoid Arthritis

BEFORE TREATMENT:
Periarticular swelling and hydrarthrosis

AFTER TREATMENT:
Diminution of pain, increased mobility, and visibly decreased effusion and swelling

Rehabilitation Achieved Through Conservative Dosage

Management in Everyday Practice

The use of simple laboratory tests (sedimentation rates, urinalyses, blood counts, blood pressure, and frequent weight recordings), individualized adjustment of dosage, and careful clinical observation will permit most patients to benefit materially . . . without fear of undesired effects.

Effective Antirheumatic Response

Effective antirheumatic response was achieved in all 100 patients in a long-term study at the Mayo Clinic. More than 50 of these arthritics were maintained on 50 mg. or less daily. In no case was it necessary to withdraw the hormone.

Ward, L. E., Slocumb, C. H., Polley, H. F., Lowman, E. W., and Hench, P. S.: *Proc. Staff Mtgs., Mayo Clinic* 26: 361, September 26, 1951.

Literature on Request

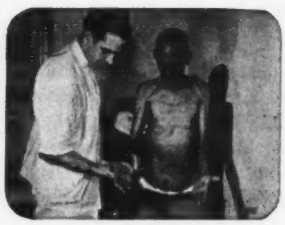
Cortone®
ACETATE
(CORTISONE Acetate Merck)

MERCK & CO., INC.
Manufacturing Chemists
RAHWAY, NEW JERSEY
In Canada: MERCK & CO. Limited—Montreal

VISUAL
SQUIBB
AIDS

SELECTED MEDICAL FILMS

...FROM THE SQUIBB MEDICAL FILM LIBRARY

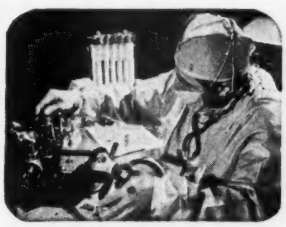


Ask Your Squibb Professional Service Representative

SQUIBB Medical Film Library offers selected motion pictures for showings at your medical group, staff meeting, or hospital—without cost or obligation.

These special films present a pictorial clinic of important medical subjects and new forms of therapy, of particular interest at medical schools, conventions, staff meetings, and to special hospital groups. Actual filming of these motion pictures was supervised by eminent medical authorities. Most films are in color, 16 mm. width, majority with sound track. Running time is from 5 to 45 minutes.

You may obtain a catalog of Squibb Medical Films from your Squibb Professional Service Representative, or by writing directly to us. Your Squibb Professional Service Representative will also obtain the films for you and handle all arrangements for the showings.



E. R. SQUIBB & SONS, 745 Fifth Avenue, New York 22, New York

THE KANSAS MEDICAL SOCIETY OFFICERS

Presidents, C. H. Benage, M.D., Pittsburg
President-elect, W. F. Bernstorf, M.D., Winfield
First Vice President, L. R. Pyle, M.D., Topeka
Second Vice Presidents, M. C. Eddy, M.D., Hays
Secretary, Dale D. Vermillion, M.D., Goodland
Treasurer, J. L. Lattimore, M.D., Topeka
AMA Delegate 1951-1953, L. S. Nelson, M.D. Salina
AMA Delegate 1950-1952, John M. Porter, M.D., Concordia

COUNCILORS AND COUNCILOR DISTRICTS

FIRST DISTRICT—W. L. Anderson, M.D., Atchison
SECOND DISTRICT—H. P. Jones, M.D., Lawrence
THIRD DISTRICT—J. G. Hughbanks, M.D., Independence
FOURTH DISTRICT—F. C. Taggart, M.D., Topeka
FIFTH DISTRICT—L. J. Beyer, M.D., Lyons
SIXTH DISTRICT—J. V. Van Cleve, M.D., Wichita
SEVENTH DISTRICT—Severt A. Anderson, M.D., Clay Center
EIGHTH DISTRICT—A. E. Rueb, M.D., Salina
NINTH DISTRICT—Marion J. Renner, M.D., Goodland
TENTH DISTRICT—L. W. Reynolds, M.D., Hays
ELEVENTH DISTRICT—C. V. Black, M.D., Pratt
TWELFTH DISTRICT—R. G. Klein, M.D., Dodge City

Oliver E. Ebel, Executive Secretary — **Headquarters Office, 512 New England Building, Topeka**

COUNTY MEDICAL SOCIETIES

COUNTY	PRESIDENT	ADDRESS	SECRETARY	ADDRESS
Allen	G. B. Pees, M.D.	Iola	F. X. Lenski, Jr., M.D.	Iola
Anderson	M. J. Stevens, M.D.	Garnett	R. E. White, M.D.	Garnett
Atchison	I. R. Morrison, M.D.	Atchison	W. Spencer Fast, M.D.	Atchison
Barber	D. C. McCarty, M.D.	Medicine Lodge	H. Yasuda, M.D.	Hardtner
Barton	M. W. Carlson, M.D.	Ellinwood	A. W. Beahm, M.D.	Great Bend
Bourbon	J. R. Prichard, M.D.	Fort Scott	L. P. Randles, M.D.	Fort Scott
Brown	A. L. Nichols, M.D.	Hiawatha	R. T. Nichols, M.D.	Hiawatha
Butler	A. P. Cloyes, M.D.	El Dorado	J. M. Shields, Jr., M.D.	El Dorado
Central Kansas	J. P. Haigler, M.D.	Hays	R. H. O'Donnell, M.D.	Ellsworth
Chase			Jacob Hinden, M.D.	Strong City
Chautauqua	E. A. Marrs, M.D.	Sedan	W. B. Scimeca, M.D.	Sedan
Cherokee	C. C. Fuller, M.D.	Columbus	P. H. Grubb, M.D.	Galena
Clark	I. R. Burket, M.D.	Ashland	J. H. McNickle, M.D.	Ashland
Clay	F. C. Shepard, M.D.	Clay Center	G. B. McIlvain, M.D.	Clay Center
Cloud	L. E. Filkin, M.D.	Concordia	M. D. McComas, Jr., M.D.	Concordia
Coffey	A. N. Gray, M.D.	Burlington	A. B. McConnell, M.D.	Burlington
Comanche	R. A. J. Shelley, M.D.	Coldwater	L. G. Glenn, M.D.	Protection
Cowley	H. H. Jones, Sr., M.D.	Winfield	A. Y. Wells, M.D.	Winfield
Crawford	P. B. Leffler, M.D.	Pittsburg	E. E. Miller, M.D.	Pittsburg
Dickinson	D. C. Chaffee, M.D.	Abilene	C. R. Svoboda, M.D.	Chapman
Doniphan	A. E. Cordonier, M.D.	Troy	Ralph R. Clutz, M.D.	Bendena
Douglas	J. A. Holmes, M.D.	Lawrence	G. E. Manahan, M. D.	Lawrence
Edwards	Rene Schnoebelen, M.D.	Kinsley	F. G. Meckfessel, M.D.	Lewis
Elk	Frank L. DePew, M.D.	Howard	J. Gordon Claypool. M.D.	Howard
Finney	J. O. Austin, M.D.	Garden City	J. W. Turner, M.D.	Garden City
Ford	A. B. Busch, M.D.	Dodge City	C. M. Alderson, M.D.	Dodge City
Franklin	L. N. Speer. M.D.	Ottawa	R. S. Roberts, M.D.	Ottawa
Geary	R. M. Carr, M.D.	Junction City	C. V. Minnick, M.D.	Junction City
Greenwood	John H. Basham M.D.	Eureka	James J. Basham, M.D.	Eureka
Harper	L. C. Joslin, M.D.	Harper	P. G. Miller, M.D.	Anthony
Harvey	W. C. Dreese, M.D.	Halstead	A. S. Hawkey, M.D.	Newton
Jackson	E. C. Moser, M.D.	Holton	Roy H. Moser, M.D.	Holton
Jefferson	W. L. Good, M.D.	Perry	C. J. Bliss, M.D.	Perry
Jewell	C. S. Hershner, M.D.	Esbon	R. M. Owensby, M.D.	Mankato
Johnson	G. R. Maser, M.D.	Mission	A. E. Derrington, M.D.	Mission
Kingman	T. L. Waylan, M.D.	Nashville	H. E. Haskins, M.D.	Kingman
Labette	C. F. Henderson, M.D.	Parsons	H. A. Burnett, M.D.	Parsons
Leavenworth	M. A. Rabe, M.D.	Leavenworth	Vincent Christ, M.D.	Leavenworth
Lyon	F. J. Eckdall, M.D.	Emporia	W. E. Luedtke, M.D.	Emporia
McPherson	E. C. Bransted, M.D.	McPherson	A. H. Dyck, M.D.	McPherson
Marion	R. R. Melton, M.D.	Marion	C. R. Magee, M.D.	Marion
Marshall	V. J. Vaughn, M.D.	Axtell	R. D. Hughes, M.D.	Frankfort
Meade-Seward	D. G. Holcomb, M.D.	Liberal	A. L. Hilbig, M.D.	Liberal
Miami	W. L. Speer, M.D.	Osawatomie	William Brown, M.D.	Paola
Mitchell	H. B. Vallette, M.D.	Beloit	I. F. Nienstedt, M.D.	Beloit
Montgomery	J. D. McMillion, M.D.	Coffeyville	W. T. Read, M.D.	Coffeyville
Morris	B. E. Miller, M.D.	Council Grove	N. A. Burkett, M.D.	Council Grove
Nemaha	C. C. Hunnicutt, M.D.	Sabetha	T. A. Montgomery, M.D.	Sabetha
Neosho	W. C. Weir, M.D.	Erie	F. F. Ewen, M.D.	Chanute
Northwest Kansas	C. E. Sixbury, M.D.	Oberlin	D. E. McCoy, M.D.	Oberlin
Osage	P. D. Adams, M.D.	Osage City	F. M. Smith, M.D.	Lyndon
Osborne	W. W. Miller, M.D.	Osborne	I. E. Henshall, M.D.	Osborne
Pawnee	O. R. Cram, M.D.	Larned	H. L. Patterson, M.D.	Larned
Pottawatomie	L. W. Cazier, M.D.	Wamego	E. A. Walsh, M.D.	Onaga
Pratt	M. E. Christmann, M.D.	Pratt	R. W. Edwards, M.D.	Pratt
Reno	R. W. Fernie, M.D.	Hutchinson	W. E. Brownlee, M.D.	Hutchinson
Republic	C. V. Haggman, M.D.	Scandia	P. L. Beiderwell, M.D.	Belleville
Rice	A. F. Schmidt, M.D.	Little River	E. R. Hill, M.D.	Lyons
Riley	T. H. White, M.D.	Manhattan	H. P. Jubelt, M.D.	Manhattan
Rush-Ness	W. J. Singleton, M.D.	LaCrosse	R. E. Grene, M.D.	LaCrosse
Saline	L. W. Hatton, M.D.	Salina	J. C. Mitchell, M.D.	Salina
Sedgwick	B. P. Meeker, M.D.	Wichita	W. H. Fritzemeier, M.D.	Wichita
Shawnee	B. J. Ashley, M.D.	Topeka	D. B. Foster, M.D.	Topeka
Smith	F. H. Relihan, M.D.	Smith Center	Victor E. Watts, M.D.	Smith Center
Stafford	F. W. Tretbar, M.D.	Stafford	O. W. Longwood. M.D.	Stafford
Sumner	K. E. Voldeng, M.D.	Wellington	W. M. Cole, M.D.	Wellington
Washington	D. A. Bitzer. M.D.	Washington	L. L. Huntley, M.D.	Washington
Wilson	D. C. Smith, M.D.	Fredonia	C. E. Stevenson. M.D.	Neodesha
Woodson	A. C. Dingus, M.D.	Yates Center	H. A. West, M.D.	Yates Center
Wyandotte	E.J.Grosdidier,M.D.	Kansas City	G. R. Peters, M.D.	Kansas City

Ideal
Infant Feeding
Formula

S-M-A®

S-M-A is a complete formula.

Unmatched in similarity to healthy mother's milk, S-M-A provides all essential food elements, including vitamins and minerals well in excess of recommended daily allowances.

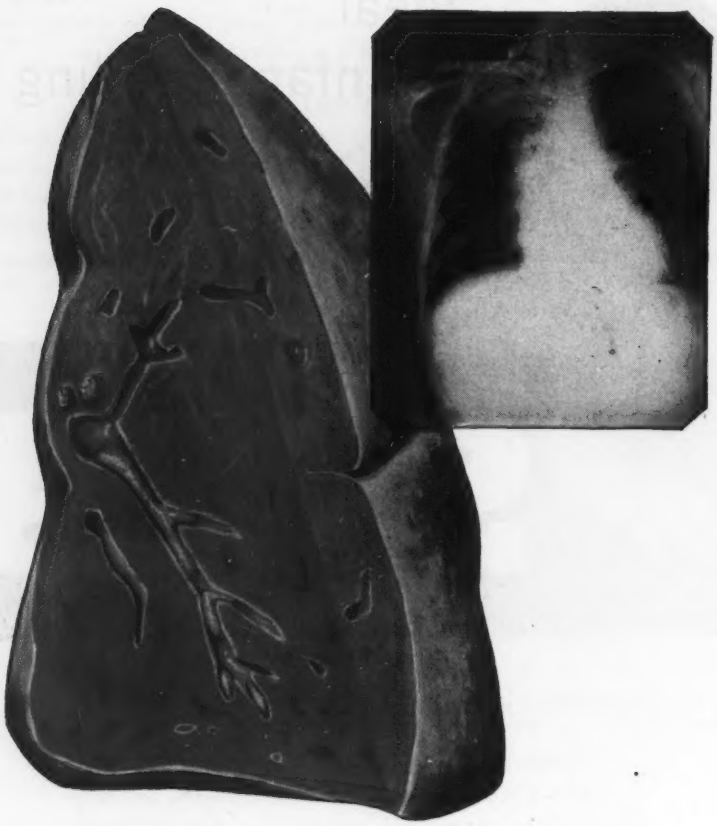
S-M-A is an economical formula.

Only water need be added. Since the addition of nutritive elements is unnecessary, *the initial cost is the whole cost*. And the whole cost of the complete S-M-A formula is *less than 1¢ per ounce*.

S-M-A Liquid **S-M-A** Powder

Wyeth®

Wyeth Incorporated, Philadelphia 2, Pa.



in primary atypical pneumonia:

"It is our clinical impression, supported by the presented data, that terramycin is the drug of choice in the treatment of atypical pneumonia in infants and children."

Graves, F. B., and Ball, W. O.:
J. Pediat. 39:155 (Aug.) 1951

ANTIBIOTIC DIVISION Pfizer

Terramycin is also indicated in a wide range of

Terramycin
HYDROCHLORIDE
CRYSTALLINE

GRAM-POSITIVE BACTERIAL INFECTIONS

Lobar pneumonia • Mixed bacterial pneumonias
Bacteremia and septicemia
Acute follicular tonsillitis
Septic sore throat • Pharyngitis
Acute and chronic otitis media
Acute bronchitis • Laryngotracheitis
Tracheobronchitis • Sinusitis
Chronic bronchiectasis
Pulmonary infections associated with pancreatic insufficiency
Scarlet fever • Urinary tract infections
Acute and subacute purulent conjunctivitis
Acute catarrhal conjunctivitis
Chronic blepharoconjunctivitis not involving the meibomian gland
Abscesses • Cellulitis
Furunculosis • Impetigo
Infections secondary to Acne vulgaris
Erysipelas • Peritonitis

GRAM-NEGATIVE BACTERIAL INFECTIONS

Gonorrhea • Brucellosis
Bacteremia and septicemia
Friedländer's pneumonia
Mixed bacterial pneumonias
Pertussis • Diffuse bronchopneumonia
Post-partum endometritis • Granuloma inguinale
Dysentery • Urinary tract infections
Respiratory tract infections
Cellulitis • Peritonitis • Tularemia

SPIROCHETAL INFECTIONS

Syphilis • Yaws • Vincent's infection

RICKETTSIAL INFECTIONS

Epidemic typhus • Murine typhus
Scrub typhus • Rickettsialpox
Q fever • Rocky Mountain spotted fever

VIRAL INFECTIONS

Primary atypical pneumonia (virus pneumonia)
Lymphogranuloma venereum • Trachoma

PROTOZOAL INFECTIONS

Amebiasis

Available as

CAPSULES
ELIXIR
ORAL DROPS
INTRAVENOUS
OPHTHALMIC OINTMENT
OPHTHALMIC SOLUTION

ACCEPTED COUNCIL ON PHARMACY AND CHEMISTRY AMERICAN MEDICAL ASSOCIATION

CHAS. PFIZER & CO., INC., *Brooklyn 6, N.Y.*

Meat and its Important Contribution of Essential Minerals

With the exception of calcium and iodine,[1] meat, as customarily consumed, makes an important contribution to the mineral needs of the American people. Its minerals include those needed in substantial amounts as well as those needed in trace amounts only.

The array of data listed below gives the approximate amounts of essential minerals provided by muscle meat when seven ounces per day are consumed.[1] The minerals include those now known to be essential components of the human organism—the skeletal framework and teeth, soft tissue structures including blood, and substances concerned in regulatory functions.

APPROXIMATE MINERAL CONTENT OF MEATS

200 Gm. (approx. 7 oz.),[1] Edible Portion (Uncooked)

	Beef Round	Lamb Leg	Pork Loin	Veal Shoulder
Minerals, total[2]	2.0 Gm.	1.8 Gm.	1.8 Gm.	2.0 Gm.
Calcium[3]	22 mg.	20 mg.	20 mg.	22 mg.
Chlorine[3]	147 mg.	136 mg.	125 mg.	147 mg.
Copper[3]	0.2 mg.	0.2 mg.	0.2 mg.	0.2 mg.
*Iodine[4] (Ohio animals)	0.02 mg.	0.03 mg.	Data not available	0.01 mg.
Iron[3]	5.8 mg.	5.4 mg.	5.0 mg.	5.8 mg.
Magnesium[3]	46 mg.	42 mg.	39 mg.	46 mg.
Phosphorus[3]	360 mg.	426 mg.	372 mg.	398 mg.
Potassium[3]	661 mg.	610 mg.	559 mg.	661 mg.
Sodium[3]	164 mg.	152 mg.	139 mg.	164 mg.
†Cobalt[5]	0.0002 mg.	———	Data not yet available	———
†Manganese[3]	0.03 mg.	0.03 mg.	0.02 mg.	0.03 mg.
†Zinc[5]	9.4 mg.	———	Data not yet available	———

*Iodine content of meat varies with the iodine content of feed of the animals.
†Needed in trace amounts only.

The average values for iron, phosphorus, and copper of the four kinds of meat shown constitute about 46, 25, and 100 per cent, respectively, of the National Research Council's recommended daily allowances for adults, and the average values for chlorine, potassium, and sodium constitute about 14, 63, and 16 per cent, respectively, of the estimated daily adult needs, as based on mineral balance studies.[6] Although no specific information is available on the quantitative needs for cobalt, magnesium, manganese, and zinc, nutrition information would suggest that the amounts reported above have nutritional importance or significance.

In addition to its notable content of essential minerals, meat also furnishes large amounts of biologically complete protein and important amounts of vitamin B complex, which includes biotin, choline, folic acid, inositol, niacin, pantothenic acid, pyridoxine, riboflavin, thiamine, and vitamin B_{12}. On the basis of its rich contribution of nutritional essentials, meat well deserves its prominent place in the daily diet of the American people, the world's best-nourished people.

1. Recent estimates of the U. S. Department of Agriculture indicate that the per capita consumption of meat in the United States approaches seven ounces per day.
2. Watt, B. K., and Merrill, A. L.: Composition of Foods —Raw, Processed, Prepared, In Agriculture Handbook No. 8, United States Department of Agriculture, 1950.
3. Estimated on basis of protein content of meats. Sherman, H. C.: Food Products, ed. 4, New York, The Macmillan Company, 1948, p. 155.
4. Ohio animals; varies with iodine content of feed. Johnson, H. J.: Bridges' Dietetics for the Clinician, ed. 5, Philadelphia, Lea & Febiger, 1949, p. 800.
5. Mitteldorf, A. J., and Landon, D. O.: Analytical Chemistry; Spectrochemical Analysis of Beef for Mineral-Element Content, Armour Research Foundation of Illinois Institute of Technology. In Press.
6. Dauphinee, J. A.: Sodium, Potassium, and Chloride Malnutrition, Including Water Balance and Shock, in Jolliffe, N.; Tisdall, F. F., and Cannon, P. R.: Clinical Nutrition, New York, Paul B. Hoeber, Inc., 1950, p. 341.

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.

ACCEPTED COUNCIL ON FOODS AND NUTRITION AMERICAN MEDICAL ASSOCIATION

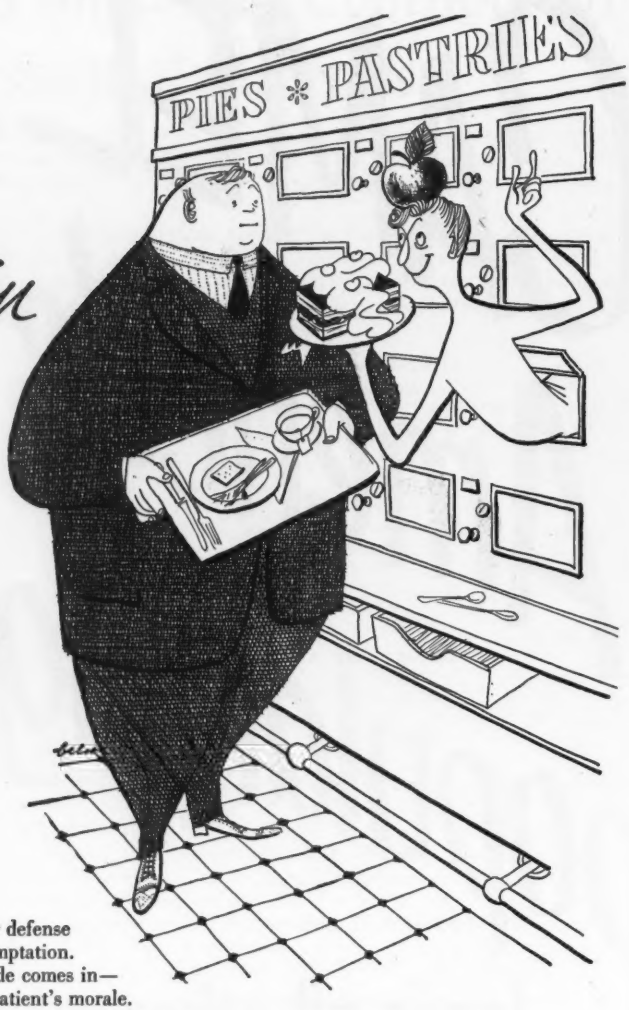
American Meat Institute

Main Office, Chicago...Members Throughout the United States

CAMEL—America's most popular cigarette

_leads all other brands by billions!

when *temptation* **pops up everywhere**



WILL-POWER alone is a poor defense against the constant prodding of temptation. That's where DESOXYN Hydrochloride comes in—curbing the appetite, uplifting the patient's morale. Weight for weight, DESOXYN is more potent than other sympathomimetic amines so that *smaller doses* can produce the desired anorexia with *a minimum of side-effects.* One 2.5-mg. or 5-mg. tablet before breakfast and another about an hour before lunch are usually sufficient. In addition, DESOXYN has a *quicker acion, longer effect.*

DESOXYN is equally effective as a valuable adjunct in depressive states associated with the menopause, prolonged illness and convalescence as well as in the treatment of narcolepsy and for adjunctive therapy in alcoholism. All pharmacies have DESOXYN in 2.5-mg. and 5-mg. tablets, in elixir form and in 1-cc. ampoules. Abbott

PRESCRIBE

Desoxyn®

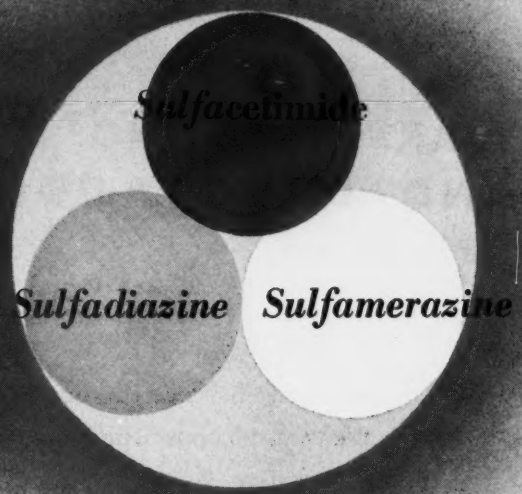
hydrochloride

(METHAMPHETAMINE HYDROCHLORIDE, ABBOTT)

SMALLER DOSAGE	QUICKER ACTION	LONGER EFFECT	MINIMAL SIDE-EFFECTS

Sulfonamide Mixture Therapy At Its Best

TRICOMBISUL



For greater clinical safety plus the advantages of more rapid absorption, better tissue distribution and faster therapeutic effect.

TRICOMBISUL Tablets, 0.5 Gm. total sulfonamides, each tablet containing 0.166 Gm. of sulfa*cetimide,* sulfadiazine and sulfamerazine.

TRICOMBISUL Liquid, 0.5 Gm. total sulfonamides (0.166 Gm. each of sulfa*cetimide* [solubilized], sulfadiazine and sulfamerazine) per teaspoonful (4 cc.).

*T.M.

Schering **CORPORATION · BLOOMFIELD, NEW JERSEY**

TRICOMBISUL

SCHERING

50 and Five

YEARS TREATING ALCOHOL AND DRUG ADDICTION

In 1897 Doctor B. B. Ralph developed methods of treating alcohol and narcotic addiction that, by the standards of the time, were conspicuous for success.

Twenty-five years ago experience had bettered the methods. Today with the advantages of collateral medicine, treatment is markedly further improved.

The Ralph Sanitarium provides personalized care in a quiet, homelike atmosphere. Dietetics, hydrotherapy and massage speed physical and emotional re-education. Cooperation with referring physicians. Write or phone.

The

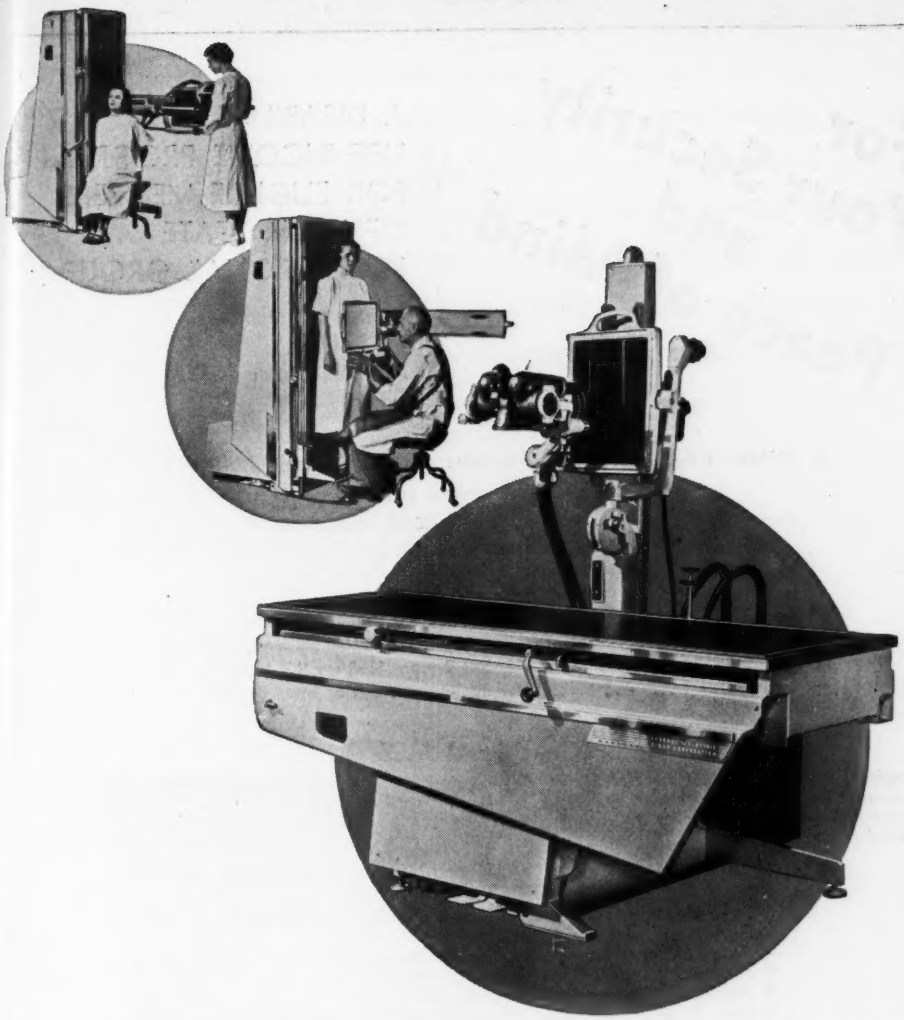
RALPH SANITARIUM

Established 1897

Ralph Emerson Duncan, M.D.
DIRECTOR

529 HIGHLAND AVENUE • KANSAS CITY 6, MISSOURI

Telephone Victor 3624



ONE TUBE DOES DOUBLE DUTY IN THIS MAXICON

Versatile is the word for this Maxicon. Capable of a wide range of diagnostic service, it has ample facilities for both radiography and fluoroscopy, horizontaliy and vertically.

Hand-tilt or motor-driven, the single-tube radiographic and fluoroscopic table is designed for operation with 100 or 200 ma generators. Its table-mounted tube stand makes it compact — ideal for small room.

See your x-ray representative or write X-Ray Department, General Electric Company.

GENERAL ELECTRIC

Direct Factory Branch: **1114 Grand Avenue, KANSAS CITY, MO.**

For Your Security and Peace of Mind

A DISABILITY LIFE INCOME PROGRAM FOR ELIGIBLE MEMBERS OF YOUR STATE PROFESSIONAL GROUP

Lifetime Protection for both Sickness & Accidents

A SILENT PARTNER . . . ***Continental's Companion Policies***

ACCIDENT AND CONFINING SICKNESS

Pays $	400	Monthly Benefits first 2 years ($200 1st mo.) and
$	300	Monthly Benefits thereafter for life.
Pays $	600	Additional Monthly Benefits First 3 Months for Hospital Disability.
Pays $	7,500	Accidental Death Benefits, $12,500 Double Indemnity.
Pays $	10,000	Loss of Hands, Feet or Eyes, $15,000 Double Indemnity (or)
$	5,000	Cash, & $400 monthly first 2 years, $300 monthly thereafter. Adjusted benefits for disabilities occurring after age 60.

SPECIAL FEATURES

No Cancellation Clause,—Standard Provision 16
No Terminating Age,—Standard Provision 20
No Increase in Premium,—Once Policy is Issued
Grace Period 15 Days

Non Pro-Rating,—Standard Provision 17
Non-Assessable,—No Contingent Liability
Non-Aggregate,—Previous Claims Paid do not limit Company's Liability

Unusually Complete Protection

★ Pays Monthly Benefits from 1st Day to Life.
★ Pays Benefits for both Sickness and Accident.
★ Pays Lifetime Benefits for Time or Specific Losses.
★ Pays Regular Benefits for Commercial Air Travel.
★ Pays Benefits for Non-Disabling Injuries.
★ Pays Benefits for Non-Confining Sickness.
★ Pays Benefits for Septic Infections.
★ Pays Whether or not Disability is Immediate.
★ Waives Premiums for Total Permanent Disability.
★ Renewal is guaranteed to individual active members, except for non-payment of premium, so long as the plan continues in effect for the members of your designated organization.

CONTINENTAL CASUALTY COMPANY

PROFESSIONAL DEPARTMENT, *Intermediate Division*

30 EAST ADAMS STREET—SUITE 1100—CHICAGO 3, ILLINOIS

Also Attractive Health With Lifetime Accident Policy I.P.-1327 For Ages 59 to 75

Name.....

Address.....

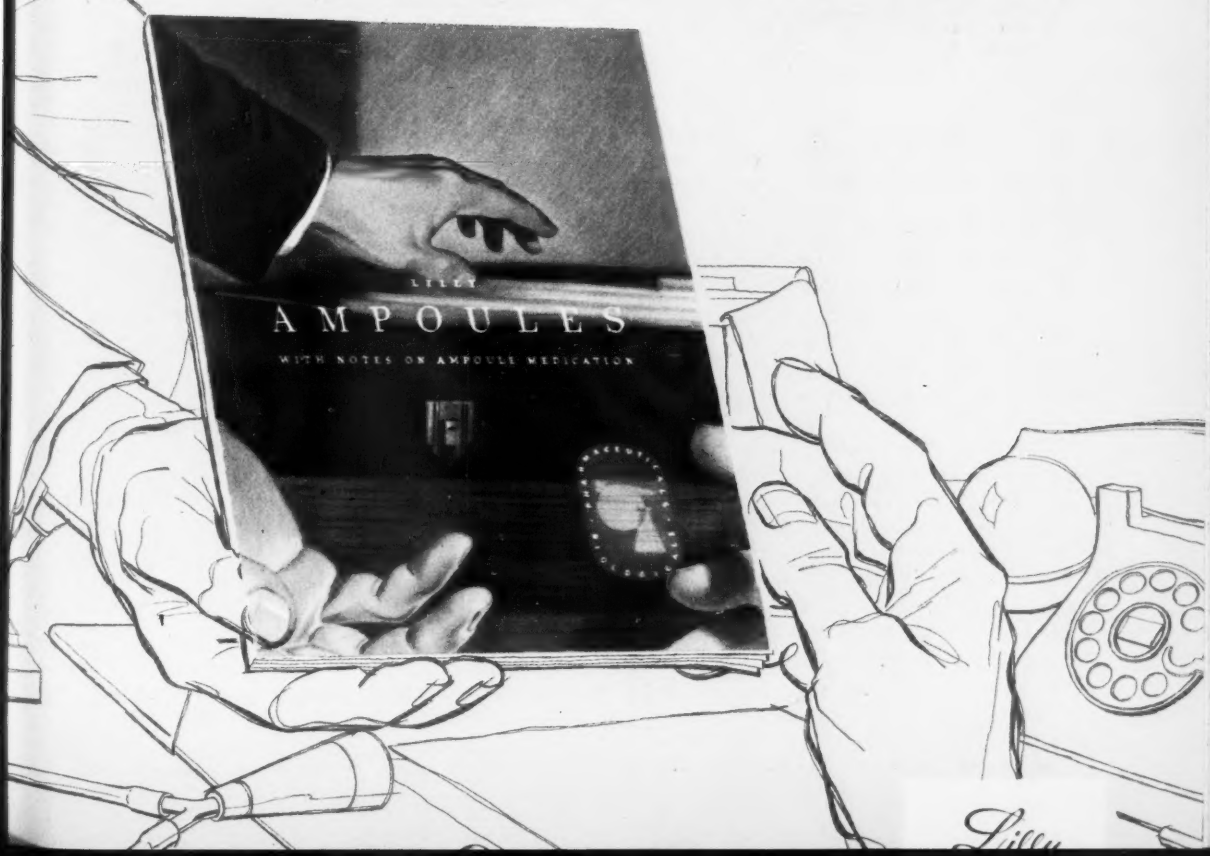
Age.....

NOTICE—**Only Companion Policies GP 1309 and IP-1308 pay the above benefits.**
IMPORTANT—Permit no agent to substitute—IMPORTANT

Like every doctor, he finds it necessary to regulate his time with care. Because the representatives of pharmaceutical houses are usually trained to condense useful information, Dr. Harris regularly sees those men whose visits he has found to be worth his time. They save him hours of reading about pharmaceutical developments which can help him practice better medicine. In two minutes, for example, Dr. Harris received the following useful facts from a medical service representative who had spent many hours studying and condensing material in order to report that . . .

Doctor Harris—

here's the latest



'Amphedroxyn Hydrochloride' offsets fatigue
(METHAMPHETAMINE HYDROCHLORIDE, LILLY)

It has been demonstrated with human subjects that 'Amphedroxyn Hydrochloride,' by imparting a sense of increased energy, delays fatigue. This property enhances the usefulness of the drug which is used primarily to combat obesity by curbing the appetite. Although its potency permits it to be used at less frequent intervals than amphetamine, 'Amphedroxyn Hydrochloride' produces relatively few undesirable side-effects.

Lilly ELI LILLY AND COMPANY · INDIANAPOLIS 6, INDIANA, U. S. A.

THE JOURNAL
of the
KANSAS MEDICAL SOCIETY
Owned and Published by The Kansas Medical Society

Volume LIII MARCH, 1952 No. 3

A Working Program for the Care and Treatment of the Hypertensive Patient

E. Grey Dimond, M.D.*

Kansas City, Kansas

A discussion regarding the treatment of essential hypertension must be predicated on the assumption that we are speaking of the type of hypertension which is generally seen and not the hypertension associated with coarctation of the aorta, pheochromocytoma, adrenal or pituitary tumors, or remediable renal disease. The importance of differentiating these various forms of hypertension is apparent and the differentiation usually not difficult. Although it is true that the vast majority of individuals will be essential hypertensives and it is but the rare patient who will have a pheochromocytoma, certainly every patient with essential hypertension should have a benzodioxane test or some other test for an adrenal medullary cause for hypertension. The simple habit of palpating the pulse in the feet will serve to eliminate hypertension due to coarctation of the aorta.

The treatment of hypertension lies not in medicines nor in surgery for the vast majority of individuals. The great percentage of patients with hypertension will live out their lives to pass on from some other disease, or perhaps if they have been fortunate they will never have known they have hypertension and will never have been subjected to treatment.

There is a much smaller group of unfortunate individuals whose elevation in blood pressure will be so severe as to be dangerous. The disease will be so destructive that over 50 per cent of this group will die from either a coronary occlusion or cardiac failure. Of the remaining, 40 per cent will die from central nervous system complications and 10 per cent will die in uremia. It is toward this group that the following comments are directed.

Good, practical, across-the-desk psychiatry is the most generally successful treatment for early hypertension. The use of barbiturates must be controlled by the physician. He must be careful that his patient does not gradually need additional doses until he has also added night-time seconal to his medications and is in danger of becoming habituated. The amount of phenobarbital necessary can be tempered greatly by insisting that the patient modify his daily activities, arranging for adequate periods of rest and relaxing hobbies. For the competitive type of personality that the average hypertensive seems to have, poker and bridge are certainly tensive experiences and should be cautioned against. Interrupted medication with phenobarbital is a proper and conservative method of administration, the drug being interrupted for a week or two after a similar period of administration. A great deal of phenobarbital is dispensed carelessly, without proper regard for the long range welfare of the patient.

For those individuals in whom there is evidence that the elevated blood pressure is steadily progressing and that the vascular symptoms are increasing, the next treatment to be utilized is some form of veratrum viride. Several commercial products are available, none of which is ideal and all of which will probably be replaced in the near future. Vertavis is a crude form of veratrum viride which has had considerable clinical trial and is undoubtedly successful in a certain number of patients. It is economical and practical to use, but must be used with constant supervision. The effective dose is close to being a nauseating dose, and many individuals cannot take it because of vomiting. Veraloid is an extract of veratrum viride, probably a purer preparation than vertavis, and individuals unable to tolerate vertavis should be given a definite trial on veraloid. Phenobarbital can be used concurrently. It is not uncommon for a patient to obtain results for a

*Director, Cardiovascular Laboratory, University of Kansas School of Medicine, Kansas City, Kansas.

while on the drug and then become resistant to it. However, the drug can be re-established after a period of rest and may again be found efficacious.

However, these drugs are not ideal for the chronic management of hypertension. Autonomic nervous system blocking, dispensed under such various trade names as etamon, dibenamine, regitine, etc., are uniformly of no practical value in the management of chronic hypertension. However, the veratrum products and the blocking agents are useful in the management of the patient with hypertensive encephalopathy or in attempting to stabilize the malignant hypertensive prior to surgery. I have used a veratrum product, veratrone, in hypertensive encelphalopathy and toxemia of pregnancy with good result. The present status of any of these drugs in the chronic management of hypertension is limited but should be given a trial.

For that group of patients failing to benefit from these measures, there is definite evidence to indicate that sodium restriction can benefit a considerable number. This requires closer adherence to dietary restriction than is generally followed. It has been definitely shown that certain individuals will not have a decrease in their diastolic pressure until they have cut their sodium intake to as low as 200 milligrams a day. This requires a careful appraisal of the diet with consultation with the wife and careful dietary instruction. The importance of the diet must be impressed upon the individual because he will be most recalcitrant after a few days on the diet. Unless he has a sincere desire to maintain the regimen, the procedure is useless. A trial of at least one month would be necessary to establish the results adequately. A simple office procedure, such as the bedside chloride test,[1] should be used to test for chloride in the patient's urine.

For those individuals not benefiting from sedation, veratrum viride, and salt restriction, it is worthwhile to try the rice diet as described by Kempner. This is not recommended with the viewpoint that rice itself is a specific therapy but rather because this diet offers a simple means of giving a low sodium, low animal protein, low cholesterol, reducing diet. Due consideration must be given to the fact that many of Kempner's claims have *not* been disproved. Although it is generally felt that the diet is effective because of sodium restriction, this theory is not agreed upon by all careful students of the subject. In fact, there are just enough patients who, inexplicably, respond to the rice diet, that anyone with progressive disease deserves giving it a trial.

The combination spa-revival camp atmosphere of the rice houses at Durham, North Carolina, cannot be equalled by the family physician, but at least a positive enthusiasm must be demonstrated by the doctor when he prescribes this diet. This enthusiasm undoubtedly will have some immediate reassuring effect on the patient; but more than this, it is necessary in order to keep the patient on such a Spartan menu. The wife's help must be enlisted and considerable thought given to devising clever alterations of the monotonous diet. Before the diet is given, the patient must be prepared psychically so that he is actually anticipatory and even eager to try it. This is important inasmuch as continuous limitation of the daily intake to fruit, fruit juices, and rice is a distressing experience, and the patient will need all the encouragement and moral support that he can obtain to stay on the diet. The patient's relatives should be warned that their encouragements are necessary in order for the patient to persevere.

While on the rice diet the patient should receive iron and vitamin preparations. Kempner has recommended at least a six months trial before deciding if the diet is effective. Six weeks to eight weeks is probably long enough. There is adequate evidence to indicate that in a certain number of patients there will be a definite fall in the diastolic pressure.

Unfortunately there will be other individuals for whom the previous procedures will have no effect and whose course will be steadily downhill with evidences of vascular deterioration. For these individuals, sympathectomy must be considered and considered seriously. At present there are three forms of sympathectomy in vogue, the Peete, the Smithwick, and the Grimson. The Smithwick operation has had probably a greater amount of study. It consists of a two-stage, bilateral operation, above and below the diaphragm, with the removal of the sympathetic nervous system from approximately T-7 to L-3. Although the majority of individuals will have a return of blood pressure to hypertensive levels after two or three years, nevertheless during that period of time the individual has been spared the ravages of disease. It is very possible also that he no longer is able to hyper-respond to certain stimuli. In other words, he loses the ability to have hypertensive peaks.

Sympathectomy need not be eliminated for those individuals who already have severe vascular disease. Definite evidence shows that these people may be given a reprieve of several years.[2]

It is a grave error to recommend a sympathectomy without also carefully informing the family of the occasional undesirable results. I have had patients obtain a persistent fall in blood pressure but have such severe back pain that they considered the operation unsatisfactory. Patients must also be warned of the possible loss of ejaculatory power.

In recent months it has been definitely established

that by carefully using cortisone, DOCA, and salt, an individual can be well maintained after the surgical removal of both adrenals. Thus the hypotensive state of Addison's disease can be produced and the patient maintained in a state of well being by proper restorative therapy. This form of surgical treatment of severe hypertension seems to be beginning a popular vogue. It is very possible that until some medical treatment such as Schroeder's suggestion of 1-Hydrazinophthalazine and Hexamethonium is developed, adrenalectomy will be the most certain way of lowering blood pressure. Physicians must remember, however, that the maintenance of an adrenalectomized patient is difficult and access to adequate laboratory procedures necessary. Therefore, the procedure is not at present suitable for the majority of institutions.

It is granted that there are individuals for whom the above procedure will offer nothing and that their ultimate outcome will be death due to vascular changes from hypertension. This is true and cannot be denied. It is important to stress, however, that the physician must have a systematic, progressive form of treatment for these people; that death is not inevitable from the disease in all these individuals; that the course of the disease can be allayed; and that useful years can be added. Although the majority will not be cured, it is important to remember that palliative therapy is good therapy and often a delay in the progress of the disease will permit survival of the patient until such time as some more efficacious form of treatment is available.

Bibliography

1. Scribner, B. H.: Bedside Determination of Chloride: a Method for Plasma, Urine and Other Fluids and Its Application to Fluid Balance Problems. Proc. Staff Meeting, Mayo Clinic. 25:209, 1950.

2. White, Paul D., Dimond, E. Grey, Williams, Armistead: Follow-up Study of One Hundred Private Hypertensive Patients with Cardiovascular Complications. Journ. American Medical Association. 143:1311, 1950.

Surgical Injuries of the Urinary Tract

Raymond W. Stockton, M.D.,* and Robert H. Owens, M.D.**

Kansas City, Kansas

The urinary tract, unusually well protected by nature from trauma, is frequently the site of injury during abdominal and pelvic surgery. Unfortunately, many of these injuries occur during elective surgical procedures. The surgeon finds that, rather than helping his patient, he has corrected a relatively benign condition only to substitute a lesion that may be a source of pain and annoyance to his patient for years and may finally result in the loss of vital renal function.

It is the purpose of this paper to point out those procedures during which such injuries commonly occur, the types of injuries that may be encountered, the principles of treatment of these injuries, and prophylactic measures by which some of these lesions may be avoided.

It will be noted that no mention is made of surgical injury to the kidney as, due to the anatomic exclusion of this organ from the common operative fields, this complication is extremely rare.

Surgical Injury to the Ureter

The ureters are especially vulnerable to injury at the time of total hysterectomy. There are many other surgical procedures which endanger the ureters and, with the more radical pelvic surgery which is being performed for cancer, ureteral injuries become increasingly important. Injury to the ureter may occur by tearing, cutting, clamping, suturing, or puncturing. In spite of the type of injury, the important thing is early recognition so that proper treatment may be instituted as soon as possible. Early recognition is not always easy and secondary urinary complications may result.

Rusche and Bacon,[2] in reviewing 50 cases of ureteral injury, listed the following surgical procedures as most commonly associated with ureteral injury:

1. Gynecological
   a. Hysterectomy and oophorectomy (ovarian tumors)
   b. High forceps and breech delivery
   c. Colporrhaphy
2. General surgery
   a. Sigmoid and rectal surgery
   b. Appendectomy

During gynecological surgery, ureteral injury most often occurs during clamping of the uterine artery at the level of the internal os.

We should like to discuss the diagnosis and treatment of such injuries and to critically review nine such cases. In this series we have divided the cases

*Instructor in Urology, University of Kansas Medical Center, Kansas City, Kansas.

**Resident in Urology, University of Kansas Medical Center, Kansas City, Kansas.

CHART NO. 1

Ureteral Injury Recognized at the Time of Surgery

Patient	*Primary Disease*	*Operation and Findings*	*Post-op. Complications*	*Urological Intervention*	*Comment*
L.R.	Ca. cervix	Ca. involving uterus rt. ureter and bladder—Total Hysterectomy, partial Cystectomy and ligation of rt. ureter	11-19-50—Temp. 106° Severe rt. flank pain. 11-20-50—Temp. 105° Pain and mass in rt. flank	11-20-50—Right Nephrectomy and Ureterectomy Cortical abscess of kidney found at operation	Normal Pre-op. pyelograms and sterile urine
G.H.	Pseudo-mucinous cystadenoma of left ovary	Cystic mass involving intestines and left ureter— Oöphorectomy Colostomy Ligation of left ureter	1-14-51—Urine loaded with pus. 1-17-51—Pneumonia, left base	None	Direct ligation of ureter without complications
R.S.	Intra-ligamentous Sarcoma of uterus	Mass in rt. broad ligament— Ureter avulsed 4 cm. from renal pelvis during total Hysterectomy	Febrile 4-5 days	Immediate Nephrectomy	Immediate Nephrectomy without complications

into those not recognized at the time of surgery and those which were recognized at the time of surgery.

The above cases were all recognized at the time of surgery. This, unfortunately, is a smaller group than the unrecognized injuries. In Holloway's series of nine cases, only two were recognized at the time of surgery. The recognized injuries frequently occur in extensive surgery where conservative measures are difficult or impossible. For this reason, no example of a conservative manner of treatment is recorded in this series.

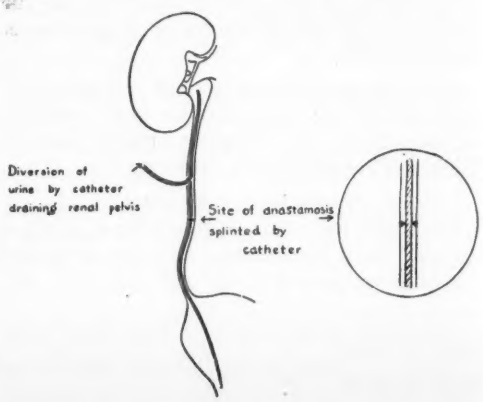
If injury should occur by clamping or inclusion of the ureter in a suture, the clamp or suture should be removed and a ureteral catheter left indwelling through the site of injury for 72 hours. There is a definite element of risk in maintaining the ureteral splint for a longer period than this as evidenced by several cases on record in which the splinting catheter eroded through the ureteral wall and into the iliac vessels, resulting in fatal hemorrhage before the complication was recognized. If the area of damage is either too large or is necrotic, then direct anastomosis of the freshened edges may be performed.

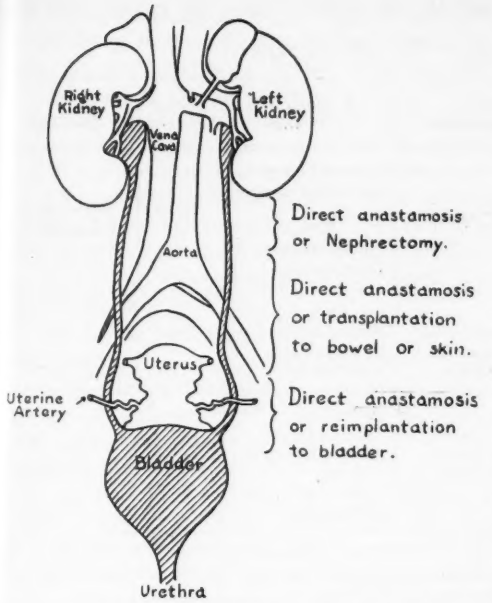
This is done over a ureteral catheter using fine silk suture which extends through all the layers except the mucosa. An extraperitoneal drain is then placed to the site of anastomosis and removed on the ninth postoperative day. It is also important that the closure not be made under tension.

If the injury has occurred to the lower one-third of the ureter and the defect is too large for direct anastomosis, the stump of the ureter may be reimplanted into the dome of the bladder. This is an excellent procedure and will conserve vital renal tissue. The bladder flap method as described by Ockerblad[3] will sometimes permit this solution of the problem when the ureter is of insufficient length for anastomosis to the bladder without tension.

When the injury is extensive, more radical procedures have to be performed. The simplest method is to ligate the end of the ureter and allow the kidney to undergo autonephrectomy. In a poor risk patient this has the great advantage of being rapid. There are, however, three main objections which must be considered:

1. If the kidney is infected the patient will develop a severe pyonephrosis in spite of chemotherapy, and emergency nephrectomy may be necessary.





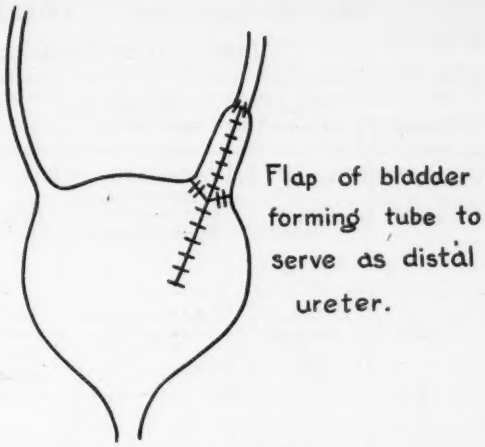
2. Vital renal tissue will be sacrificed and, without knowledge of the function of the other kidney, the life of the patient may be endangered or shortened.

3. Any attempt at later reconstructive procedure is lost.

Case 1 graphically illustrates the first objection to this procedure. In spite of the fact that the preoperative urine culture was negative and excretory urograms were reported as normal, the patient developed a severe obstructive pyonephrosis and septicemia. This necessitated a secondary nephrectomy, thus subjecting the patient to two major procedures in three days. In Case 2, ligation resulted in a smooth postoperative course with complete recovery of the patient.

If the continuity of the ureter cannot be reestablished, the safest procedure is cutaneous ureterostomy. This is a relatively rapid and simple procedure. By leaving an indwelling catheter in the renal pelvis, adequate drainage is assured. It has been suggested that, if ligation is performed, the ureter should be brought out extraperitoneally and left in the subcutaneous tissue with the ligature extending out through a stab wound. In this way, if an obstructed pyonephrosis should occur, the ureter will be easily mobilized and drainage may be instituted by inserting a catheter into the pelvis of the kidney.

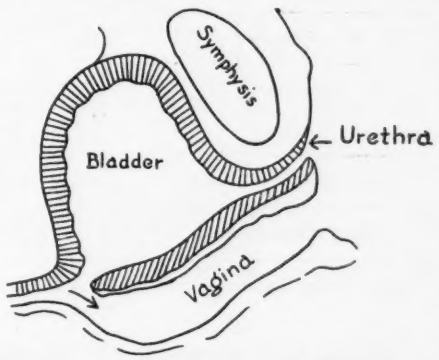
Uretero-ureterostomy has been advocated but is a poor alternative. By anastomosing one ureter to the other the function of both kidneys may be disturbed, either by stricture at the site of anastomosis or by



chronic infection. If total destruction of the ureter occurs the only alternative is immediate nephrectomy or nephrostomy. In Case 3 the ureter was avulsed four centimeters from the renal pelvis and any reconstructive procedure was impossible. An immediate nephrectomy was performed with an uneventful convalescence.

Unidentified injuries to the ureter usually lead to late urological sequelae. In Case 1 (Chart 2) the ureter had evidently been partially ligated six centimeters above the ureteral orifice. The involved kidney showed impaired function on I. V. pyelograms, but urine was still being excreted from the left ureter. With conservative management the patient had an uneventful recovery and the pyelograms returned to normal within three months. This could be explained either by absorption of a catgut ligature or resolution of edema around the site of trauma.

The more common result is the development of a uretero-vaginal fistula. Cases 2, 3, 4, and 5 are all examples of this complication. It will be noted that all patients had hysterectomy with unrecognized ureteral trauma. From three to 14 days postoper-



Uretero-vaginal fistula

CHART NO. 2

Ureteral Injuries Not Recognized at the Time of Surgery

Patient	*Primary Disease*	*Operation and Findings*	*Post-op. Complications*	*Urological Intervention*	*Convalescence*	*Comment*
K.R.	Fibroid uterus	6-28—Total Hysterectomy Left ovary adherent to uterine wall	Moderate pain in left flank	6-28—IVP's—Impaired function on left 7-2—Retro-obstruction at 6 cm. on left	Good	No surgical intervention
N.O.	Adeno-carcinoma uterus	12-16-48—Total Hysterectomy	Post-op. drainage of urine from vagina left pyonephrosis	3-2-49—Reimplantation of left ureter into bladder	Good	
N.H.	Menorrhagia	2-7-44—Total Hysterectomy	Post-op. urinary drainage from vagina	IVP—Left hydronephrosis Retro-obstruction at 6 cm. 4-16—Left Nephrectomy	Good	
L.M.	Myoma of uterus Chronic Oöphoritis	7-28—Total Hysterectomy	Post-op. urinary drainage from vagina	Same as above except obstr. at 3 cm. 10-6-48—Nephrectomy	Good	
D.S.	Adeno-carcinoma of uterus	4-22-49—Panhysterectomy	Post-op. urinary drainage from vagina	IVP—Early hydro. Left with visualization of vagina 6-10-49—Left Nephrectomy	Good	Pelvis negative on 11-11-50
D.W.	Squamous cell carcinoma of cervix	Pelvic Evisceration	Anuria—Non-functioning left kidney—Pre-op.	Rt. Nephrostomy	Poor	Died on 22nd Post-op. day

atively they all began to drain urine from the vagina. This symptom can occur with either vesico-vaginal or uretero-vaginal fistula. The steps in Chart 3 are taken in making the differential diagnosis.

Once the diagnosis of uretero-vaginal fistula is made, treatment must be considered. If the kidney on the involved side is still functioning, a reconstructive procedure should be planned. In Case 2

CHART NO. 3

Procedure	*Uretero-Vaginal Fistula*	*Vesico-Vaginal Fistula*
I.V. Pyelogram	Delayed function and/or hydronephrosis on the involved side	Negative
Cystoscopy	Normal bladder	Evidence of fistula
Ureteral Catheterization	Obstruction at the site of injury	Normal
I.V. Indigo carmine	No excretion from involved ureter	Normal bilateral excretion of dye from ureters
Methylene blue in bladder with vaginal pack	None appears on vaginal pack	Vaginal pack stained with dye

the lower end of the ureter was explored and a reimplantation into the bladder was performed. The area of injury is usually bound down by dense fibrous tissue as the result of periureteritis. For this reason, any closure of the fistula or local plastic repair is impossible. The most certain method of cure is nephrectomy. This should be performed only after a careful evaluation is made of the uninvolved kidney. When nephrectomy is performed as an elective procedure, mortality and morbidity are low. By removing the secreting source the fistula will close spontaneously.

The last case is included only to show the grave sequellae which are occasionally encountered by the urologist and the difficulties in management. This patient had a far-advanced carcinoma of the cervix with involvement of the left ureter and a non-functioning kidney on the left. A radical pelvic evisceration was performed and the remaining functioning ureter was transplanted into the sigmoid. This was a prolonged operative procedure accompanied by severe shock for which the patient received many pints of blood. Postoperatively she was anuric for 48 hours. The anuria could have been on the basis of pre-renal azotemia, prolonged shock with cortical ischemia, lower nephron nephrosis, or as a result of edema at the site of the anastomosis with a resultant obstructive hydronephrosis.

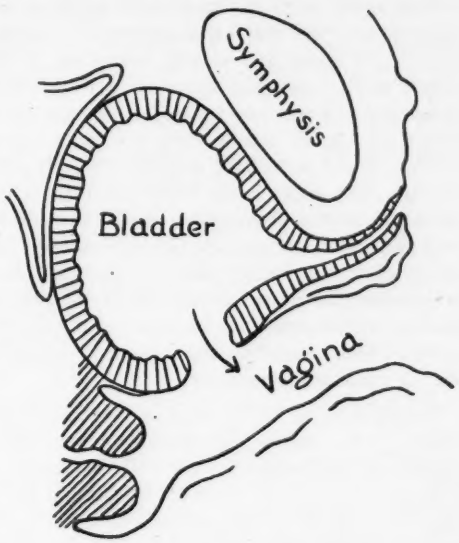
It was thought advisable to explore the right kidney. The ureter and renal pelvis were found to be dilated with 200 cc. urine. A nephrostomy was performed. The patient did secrete urine but remained oliguric and died on the 22nd postoperative day of progressive renal failure. It is probably wise to do a cutaneous ureterostomy when the disposition of a single functioning ureter is involved.

In cases of total anuria following extensive surgery in which the possibility of bilateral ureteral ligation exists, immediate cystoscopy and retrograde catheterization of the ureters should be attempted. If this complication should be found and the condition of the patient does not permit reconstructive surgery, the kidneys should be drained by nephrostomy until circumstances permit definitive surgery to reestablish urinary drainage through normal channels.

Of course, the best treatment of all is prophylaxis. The preoperative insertion of No. 6 Fr. ureteral catheters will greatly facilitate the identification of the ureters and, if injury should occur, the catheters can be used for drainage. Above all, preoperative I. V. pyelograms in cases requiring extensive surgery will give a great deal of information as to the status of the urinary tract and, if some emergency procedure has to be performed, the quality of function of the other kidney will be known.

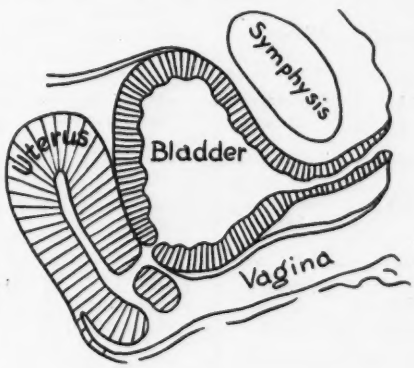
Surgical Injury to the Urethra

Surgical injury of the urinary bladder is probably a more common though usually less serious occurrence than ureteral injury and frequently befalls the practiced surgeon as well as the neophyte. Vesical damage, with or without fistula formation, may occur from an incised wound, pressure necrosis following clamping, or the pressure of retraction, or suture which has caught the bladder wall.



Vesico-vaginal fistula

These injuries most often occur during gynecological procedures such as total abdominal hysterectomy, vaginal hysterectomy, plastic operations for prolapse, and myomectomy for anterior or cervical fibroids.[5] The surgeon may fall victim to this misfortune by



Vesico-utero-vaginal fistula

incising the peritoneum with the bladder distended or adherent from previous surgery, during pelvic operations for the eradication of neoplasm such as segmental resection of the sigmoid or combined abdomino-perineal resection, or in opening a hernial sac, usually inguinal, which contains bladder. The obstetrician occasionally finds himself involved in this problem following the repair of cervical lacerations and following instrument delivery.

Here again, as in the inadvertent injury to any organ or structure, the important factor is recognition of the lesion and prompt institution of the proper therapy. Surgical injury of the bladder, if recognized and properly treated at the time of its occurrence, should usually cause no undue apprehension on the part of the surgeon. There is probably no other viscus in the body which can be injured to a similar extent and, if properly treated, present such a benign postoperative course. The ability of the bladder to heal and regenerate is so remarkable that practically the entire bladder, excluding the trigonal area, may be excised and the patient present a near-normal function and capacity within a matter of months.

Simple incision of the bladder requires merely closure with interrupted chromic catgut suture through all of the layers of the wall. Ordinarily, no attempt need be made to control bleeding in the incised wall of the bladder as approximation by the sutures and the subsequent edema will do this effectively. The sutures should not be tied so tightly that they will strangulate the intervening tissue, and a small penrose drain should be left in the prevesical space for a period of 48 hours. A No. 22 Fr. foley-bag catheter should be left indwelling and connected to under-water suction for a period of 10 days to prevent distension of the damaged viscus. In repairing any lesion in the region of the trigone one must always consider and exclude a coexisting lesion of the adjacent ureter.

Surgical violation of the bladder wall, if unrecognized and untreated, may give the signs and symptoms of extravasation of urine from any cause, i.e., progressively increasing pain in the lower abdomen, involuntary muscle rigidity, rapid pulse, fall in blood pressure, and later, urinary phlegmon with slough or fistula formation. With clinical signs and symptoms of such injury, the diagnosis may be confirmed by cystography and/or cystoscopy. If these signs have not been noted during surgery, the patient should be returned to the operating room for suprapubic cystostomy as soon as the diagnosis is made. This may be done under local anesthesia if the condition of the patient contraindicates the use of other agents. Time should not be consumed in attempting to locate and repair the site of extravasation for the cystostomy tube and a small penrose drain on either side of the bladder will provide ample drainage to allow the primary lesion to close. The drains may be removed in 72 hours and the cystostomy tube removed at the end of six days, providing drainage is assured by indwelling urethral catheter for a period of 10-14 days postoperatively.

The following tables summarize briefly six cases of surgical injury to the urinary bladder, four of which were recognized and treated at the time of occurrence.

CHART NO. 4

Bladder Injuries Recognized at the Time of Surgery

Patient	*Diagnosis*	*Operation and Findings*	*Injury to Bladder*	*Treatment*	*Post-op. Course*
A.M.	Fibroid uterus	Total abdominal Hysterectomy	Entered while incising peritoneum	Primary closure with interrupted chromic gut—8 days cath. drainage	Uneventful—Dismissed on 12th Post-op. day
J.D.	Premature Labor	Cesarean section	Laceration of dome of bladder	Primary closure with interrupted chromic gut—8 days cath. drainage	Uneventful—Dismissed on 14th Post-op. day
T.G.	Fibroid uterus	Total abdominal Hysterectomy	1½" tear in bladder	Primary closure with interrupted chromic gut—8 days cath. drainage	Uneventful—Dismissed on 13th Post-op. day
L.B.	Tubo-ovarian abscesses	Total salpingo-Oöphorectomy and total Hysterectomy	"Tear" in bladder	Primary closure with interrupted chromic gut—7 days cath. drainage	Uneventful—Dismissed on 10th Post-op. day

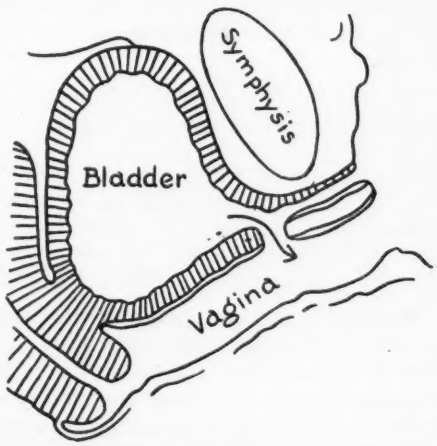
CHART NO. 5

Bladder Injuries Not Recognized at the Time of Surgery

Patient	*Diagnosis*	*Operation and Findings*	*Injury to Bladder*	*Treatment*	*Post-op. Course*
K.A.	Cervical bleeding	Total abdominal Hysterectomy	Vesico-vaginal fistula on 8th p.o. day in trigone	Closure per vagina on 16th p.o. day cath. drainage for 10 days	Repair broke down on 13th p.o. day—Pt. returned in 4 weeks and closure done per vagina
K.S.	Menorrhagia	Total abdominal Hysterectomy	Vesico-vaginal fistula noted on 9th p.o. day in bas-fond	Closure per vagina cath. drainage for 21 days	Repair broke down—Pt. returned in 8 weeks at which time closure per vagina was satisfactory

The foregoing series of cases amply demonstrates that surgical injury of the bladder which is promptly recognized and properly treated is attended by very little morbidity. On the other hand, there are few conditions that can be so exasperating to both patient and physician as the late sequelae of the unrecognized lesions. We shall not attempt to discuss in any detail the treatment of vesico-vaginal fistula. Suffice it to say that a period of at least six weeks should be allowed to elapse before surgical repair is attempted and urinary infection must be combated with antibiotics both pre and postoperatively.

By way of prophylaxis against such injuries as those described above, several simple procedures should be mentioned. An indwelling urethral catheter during surgery guards against distension with encroachment of the bladder into the operative field and prevents extravasation of large quantities of infected urine should the bladder be accidentally opened. Also, the practice of opening the peritoneum near the upper angle of the abdominal incision will occasionally prevent injury to a bladder adherent from previous surgery.[1]



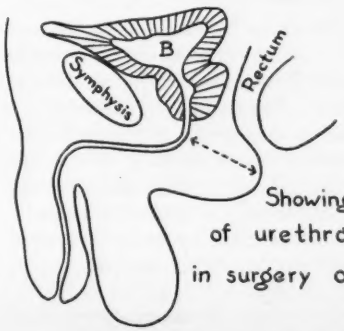
Urethro-vaginal fistula

Surgical Injury to the Urethra

Surgical injury of the urethra, fortunately, is not a common accident. The female urethra, being only approximately three centimeters in length and well protected by the pubic bones, is seldom seriously damaged except in cases of instrument delivery or operative procedures via the vaginal route. The male urethra may be damaged by surgical procedures to the perineum for any cause.

At the University of Kansas Medical Center we have on record two cases of urethral injury resulting from operation for imperforate anus in the newborn. Both of these children developed urinary fistulae requiring temporary cystostomy and periodic urethral dilatations and resulting in severe damage to the upper urinary tracts. In another instance, an adult male developed a perineal urinary fistula following combined abdomino-perineal surgery for carcinoma of the rectum which was densely adherent to the prostate. Panendoscopy revealed a small defect in the floor of the membranous urethra and this closed spontaneously around an indwelling urethral catheter.

Surgical injury of the urethra is almost invariably unrecognized at the time of its occurrence and, in the great majority of cases, results in urethro-



Showing proximity of urethra to rectum in surgery of perineum.

cutaneous fistula with attending stricture of the urethra just distal to the site of fistula formation. Reconstructive repair will often result in subsequent stricture formation at the site but, unfortunately, there is no alternative unless circumstances warrant permanent diversion of the urine by cystostomy. The repair should be done after diversion of the urine by cystostomy, and a splinting urethral catheter is left indwelling. The cystostomy tube may be removed in eight to 10 days. The urethral catheter is removed when the cystostomy wound has closed. The patient usually must return periodically for life for dilatation of the stricture which will form at the site of the urethral surgery.

Summary

The etiology, treatment, prognosis, and prophylaxis of surgical injury of the urinary tract is discussed.

Prompt recognition of the lesion and immediate institution of the proper therapy, including surgical management and adequate chemotherapy, are stressed as factors in greatly reducing morbidity and mortality from these surgical accidents.

A brief review of nine cases of ureteral injury, six cases of bladder injury, and three cases of urethral injury is presented.

Bibliography

1. Holloway, J. H.: Am. J. Ob. and Gyn., 60: pp. 30-40, July 1950.
2. Rusche and Bacon: J.A.M.A., 114-201, 1940.
3. Ockerblad, N. F.: J. Urol. 57:845-847, May, 1947.
4. Feeney, J. K.: Irish J. Med. Sc., 112-120, March, 1948.
5. Sisk, Ira.: S. G. and O., 60:857-860, April, 1935.
6. Newell, Q. V.: Ann. Surg. 109:981-986, 1939.
7. Wilson, J. M.: Urol. and Cut. Rev., 51:71-74, Feb. 1947.

Harelip and Cleft Palate: Modern Trends in Management

David W. Robinson, M.D.*

Kansas City, Kansas

The child born with a cleft defect, harelip or cleft palate, starts life with a considerable structural and functional handicap. Many children with such deformities can be aided to accept a normal station in society, but such restorations require intelligent planning and care. A skillful and individualized plan of therapy will make the difference between a fairly normal citizen or a facial, dental, or speech cripple.

The problem is not a simple one but has many facets. Surgery for the repair of cleft defects, ill-advised or poorly performed, will be the obvious cause of certain later defects. However, techniques have been so refined that a single operation for the repair of the lip is usually adequate[1, 2, 3] and a single operation restoring continuity of the palate produces a good anatomical result.

A follow-up of results by many competent surgeons has proven definite inadequacy of a routine form of treatment. Early closure of the lip, although apparently perfect in infancy or early childhood, too often later shows up such typical secondary defects[4] as the recessed flat lip that is too long; the notching or nodular protuberance of the vermillion; the flattened, lowered, drawn-out, or buckled ala nasi on the affected side; the crooked, asymmetrical, rounded or widened nose; and naso-labial fistulae. The patient, years after "successful" early closure of a cleft palate, frequently is seen for the typical late deformities of severe malocclusion, deformed teeth in a contracted recessed maxillary arch, a concave middle of the face or "dish-faced" appearance, and a tight short palate that does not produce good velar pharyngeal closure. A repaired palate may appear to be anatomically intact and long enough. The nasality in speech, however, may be so evident that even though the patient articulates well as a result of prolonged training or native intelligence and self-training, his defect is immediately obvious to his listeners.

The need for assistance in rehabilitating these children is great. Many consultants may be asked to see the individual child.[5] Not only may he have structural defects still remediable by the plastic surgeon, but his speech may be greatly improved by persistent training given by a trained speech therapist.[6] According to Oldfield,[7] "the main difficulty of the cleft palate patient is the defect in speech."

Dental caries and misshapen misplaced teeth in the contracted maxillary arch require the early services of a general dentist and orthodontist.[8, 9] Such teeth are commonly lost. A dentist trained in prosthodontia can later make an appliance to restore occlusion, to help improve the upper lip's appearance by jutting it forward, and to aid in "plugging" large perforations in the gum, upper labial sulcus,

*From the Division of Surgery, Department of Plastic Surgery, University of Kansas Medical Center, Kansas City, Kansas.

and anterior or posterior palate. In patients where it is indicated, such a prosthodontist can aid in constructing and properly fitting an adequate speech bulb appliance which allows closure of the pharynx around it for good speech.

Problems in hearing are many because these children frequently have multiple nasopharyngeal infections which secondarily produce otitis media and mastoiditis. Enlarged adenoids or tonsils may be responsible in part for this problem. Since removal of these space-filling tissues from cleft palate patients often inhibits speech, recommendation for tonsillectomy and adenoidectomy should be made after studied judgment on the part of the plastic surgeon and otolaryngologist in consultation.

Furthermore, because they do differ from their comrades, many of these children have developed certain psychological abnormalities and tend to be somewhat withdrawn from children of their own age. The services of a trained child psychiatrist may be of value in rehabilitating such children to a more normal behavior pattern.

To complete the program, a very important member of the consulting team is the pediatrician[10] whose aim is to see that the child's general health be appraised and maintained and that the child be treated as a whole, not simply as a patient or case with a cleft defect.

It would seem logical, therefore, that better treatment of these patients could be obtained by the combined teamwork of the above-mentioned specialists whose collective and studied judgment plans therapy. Such a team could study and appraise trends in treatment over the years so that it could draw some valid conclusions as to the best forms of treatment for the various types of deformities. Such an organization has been formed at the University of Kansas Medical Center and is seeing these patients at a regular time each month* on referral from their doctors.

Age of Operation

In general, it had been thought by many that babies with harelips should have their defects repaired as early as possible, providing the child is big enough to stand the surgery. For single cleft lips it was felt that a child should have normal birth weight, seven pounds or more, and for double cleft lips, should preferably weigh nine or 10 pounds. Early operation was advocated to aid in feeding, to help close the alveolar defect by the steady pressure of the gum, and for the psychological benefit to the mother.

Unilateral harelips usually can be repaired during the first few days of life so that the child can go home with the mother and be presented to the family and friends as practically a normal-appearing child. Actually the mortality for single harelip operations is quite negligible.

Surgery for a double cleft lip, however, if done in one stage is of considerable magnitude as it must be remembered that such small babies can lose only a relatively small amount of blood without jeopardizing their lives. It is doubtful that such early operation is warranted and it is rather general thinking now that, if one waits until the child is at least a few weeks old, the results are just as good and the risk to the child less. Some reassurance and explanation must be given to the parents, however, and the child will likely require more than the average amount of supervision by the attending doctor or pediatrician. Such babies may present some mechanical problem of feeding but, on the whole, if nipples with large perforations are utilized or if the babies are placed in the crook of the arm upright and fed out of a cup or small glass, these infants will receive adequate nutrition and will gain promptly. It is true that if one waits a few weeks, they will not have as good hemoglobin content and may be in somewhat more need of a small blood transfusion at the time of operation or shortly thereafter.

The current argument between reconstructive surgeons concerns itself not so much with the lip but with the time for operation on the cleft palate. Statistical evidence of performance from operations of many different techniques carried out at an early age, that is under two years, has been accumulated. There is a definite trend away from early operations on the cleft palate. The two chief detriments to the early operations are (1) inadequate growth of the middle of the face and (2) improper and inadequate speech. From clinical experience with many cases backed up by accurate cephalometric determinations of growth, it has been shown by the studies of Graber,[11] and Slaughter and Brodie[12] that early operations on the palate, even though the soft tissues alone had been shifted and manipulated, caused some interference with the centers of bony growth of the middle of the face.

Such growth studies, although far from completed, have indicated that about five-sixths of the development of the middle of the face has occurred by the age of five years and that only one-sixth of the development occurs after that. Analyses demonstrate that from the various techniques used, the most common being the Von Longenbeck palatal closure, early operation has been responsible for the recessed "dish-faced" appearance of these people who have the typical narrow, contracted, recessed maxillary arch and the shortened immobile palate. This is not universally so, and a fair percentage of

*The last Saturday morning of each month.

the patients with routine type closures in the hands of excellent surgeons have apparently normally developing faces. Adults presenting themselves with unoperated cleft defects[13] demonstrate surprisingly good facial development in contrast to many operated patients. Which type of clefts may be closed early and which late has not been definitely decided, but there is a definite trend toward delaying the operation and increasing the use of early prosthetic appliances for speech therapy.

Speech

The speech mechanism, as it is affected by early or late operation, is the other chief controversial issue in regard to the time of operation. There is a definite school of thought with considerable evidence now to back up its convictions that certain techniques of palatal closure produce a tight scarred palate for which little may ever be done to improve speech in spite of speech therapy. The foremost proponents[8] of this theory think that an obturator should be constructed early for a great number of these young patients with palatal defects and that an obturator with its speech bulb should be adjusted through the developing period of the palate and middle of the face with constant attention to speech therapy and training. These "appliance men" claim that no interference, such as is seen not infrequently following early palate repair, takes place in the development of the middle of the face and that their patients with appliances will have fairly normal faces, as well as good speech with the appliance.

There can be no question but that certain types of palatal clefts have better functional results with the use of obturators. Good speech has been reported from the use of the posterior pharyngeal flap[14, 15] and from the push-back procedure[16] but, although speech has been improved by these operations performed to lengthen the palate secondarily, this author is not overly enthusiastic. Just which of these clefts give the best ultimate functional and structural result by the use of early surgery or mechanical aids and later surgery has not been determined and may not be until after some years when large series have been studied and analyzed.

Arguments that have been presented by those advocating surgery alone as against the early use of appliances for speech are that (1) the obturator is unhygienic, (2) it requires a skilled technician to construct it, (3) constant attention is needed to see that it fits during the growing period, and (4) speech therapy must be continued over a long period of time. Further, this is a very costly method of treatment both from the standpoint of time of the prosthodontist and use of materials. Chief proponents of the appliance school claim that many of the operations apparently anatomically approximating the palate produce a tight scarred palate which can never effect velar pharyngeal closure and good speech.

Conclusions

Obviously we are in a period of change in our thinking about the proper method of therapy for cleft palate patients or, better, the individual patient. More time must elapse before the indications are clear for the type of treatment indicated for the individual patient. Such knowledge can come only through the care of a large number of patients over a prolonged period of time, studying growth development and speech mechanism as well as appearances. It is obvious that team work is needed and that the combined opinions of many specialists including the reconstructive surgeon, pediatrician, speech therapist, prosthodontist, orthodontist, general dentist, child psychiatrist, and otolaryngologist are desired. Skillful analysis after the blending of opinions of various specialists trained to solve their special problems is surely a proper approach to an unsolved problem which is definitely on its way to solution.

Bibliography

1. Blair, V. P., and Brown, J. B.: Mirault operation for single harelip. Surg., Gyn., and Obs. 51:81-98, July 1930.

2. Brown, J. B., and McDowell, Frank: Small triangular flaps for the primary repair of single cleft lips. Pl. and Reconst. Surg. No. 5:392, 1950.

3. LeMesurier, A. B.: A method of cutting and suturing the lip in the treatment of complete unilateral clefts. Pl. and Reconstr. Surg. 4 No. 1:1-13, Jan. 1949.

4. Kazanjian, V. H.: Collective Review—Secondary deformities of cleft palates. Pl. and Reconstr. Surg. Vol. 8, No. 6:497-489, Dec. 1951.

5. Cannon, Bradford: Plastic Surgery: Harelip and cleft palate. New Engl. J. of Med. Vol. 245, No. 5:179-185; No. 6:215-219, Aug. 1951.

6. Morley, Muriel E.: Cleft palate and speech. E. and S. Livingstone Ltd. Edinburgh, 1951.

7. Oldfield, Michael C.: Cleft palate and the mechanism of speech. Brit. J. of Surg. 35:173-179, Oct. 1947.

8. Cooper, Herbert K.: Cleft palate—dentistry's opportunities. J. of the Am. Dent. Assoc. 42:37-47, Jan. 1951.

9. Conroy, Cecil R.: Three age phases of orthodontic treatment of the cleft palate child. Pl. and Reconstr. Surg. Vol. 7, No. 2:100-114, Feb. 1951.

10. Coursin, D. B.: Treatment of the patient with cleft palate. Am. J. Dis. Child. 80:442-453, Sept. 1950.

11. Graber, T. M.: Craniofacial morphology in cleft palate and cleft lip deformities. Surg., Gyn. and Obs. 88:359-369, Mar. 1949.

12. Slaughter, Wayne B., and Brodie, Allan G.: Facial clefts and their surgical management in view of recent research. Pl. and Reconstr. Surg. 4:311-332, 1949.

13. Davis, Albert D.: Unoperated bilateral complete cleft lip and palate in the adult. Pl. and Reconstr. Surg. Vol. 7, No. 6:482-491, June, 1951.

14. Moran, Robert E.: The pharyngeal flap operation as a speech aid. Pl. and Reconstr. Surg. 7 No. 3:202-213, Mar. 1951.

15. Conway, Herbert: Combined use of the push-back and pharyngeal flap procedures in the management of complicated cases of cleft palate. Pl. and Reconstr. Surg. 7 No. 3:214-224, Mar. 1951.

16. Dorrance, G. M.: Cleft palate. Ann. Surg. 117:1-27, An., 1943.

Terminal Bronchiolar or "Alveolar Cell" Carcinoma of Lung: A Case Report*

H. H. Dunham, M.D., and V. G. Smith, M.D.**

Kansas City, Kansas

Terminal bronchiolar, "alveolar cell" carcinoma or pulmonary adenomatosis is a rare disease and in most of the reported cases the diagnosis has been made only by postmortem examination. Weir[1] cites references to three cases in the literature which were diagnosed antemortem on the basis of biopsy examination. This same author has reviewed 36 cases reported in the literature and has added reports on three cases. He has attempted to delineate the clinical picture on the basis of the cases reviewed. Paul and Ritchie[2] reviewed the clinical and roentgenographic characteristics of a series of cases and made the correct diagnosis in one case on the basis of such findings alone.

Good et al[3] reported eight cases in which a positive diagnosis was made by resection of a lobe or an entire lung. They also indicate that cytologic examination of sputum or bronchial secretions may offer a definite diagnosis in some cases.

Papanicolaou in a personal communication quoted by Smith, Knudtson and Watson[4] and also by Watson and Smith[5] stated that in the series of cases studied at Memorial Hospital, a large number of malignant cells were recovered in smears of sputum that showed typical cytologic changes of cancer. One of the more specific changes noted was the presence of multi-nucleated giant cells which are rarely seen in other types of carcinoma of lung. He implies the possibility that these cells are of specific diagnostic value in this lesion.

There is no record of this diagnosis at the University of Kansas Medical Center prior to August, 1951.† This paper is presented for the purpose of reporting such a case. We do not attempt to present an exhaustive review but shall discuss briefly the clinical, radiographic, and pathologic features.

Clinical Features

Weir[1] has presented perhaps the most exhaustive study of the clinical aspects of this condition. He indicates that 83 per cent of the 36 cases he reviewed were above 40 years of age. He found no occupational relationship to the malady. In general no consistent antecedent disease is reported. Cough is the most constant symptom. The cough may be dry at the onset, but later is likely to become productive of a profuse watery or frothy sputum. Indeed, the copious production of thin watery sputum is apparently a feature which is suggestive of the condition. Hemoptysis is not common and generally amounts to streaking only. Dyspnea is likely to be a prominent and not necessarily a terminal feature.

Loss of weight is common and weakness may be a prominent feature. Fever is not characteristic and when present probably indicates a complicating bronchopneumonia. Clubbing of the fingers appears to be exceptional; cyanosis is frequent as a late manifestation. The general appearance of the patients remains good, as a rule, until late in the disease. Physical examination of the chest, in most patients, shows signs of partial consolidation of the lung tissue.

Paul and Ritchie[2] stress dyspnea and cough productive of thin, watery, frothy, or mucoid sputum as outstanding clinical features in their cases. They also find hemoptysis an unimportant symptom. King and Carroll[6] are in essential agreement with other authors cited as regards the clinical picture.

Most authors regard the disease as uniformly fatal, but Good et al[3] make the reservation that surgical excision of a localized lesion may offer hope of cure. The latter group admits, however, that it is too soon to justify such a conclusion.

Roentgenologic Characteristics

Weir[1] has described the roentgenologic features as reported for 33 cases which he reviewed. He describes two general types of findings. In one type the shadows consist of multiple, small, irregular, nodular densities along with larger areas of density. In the other type single large areas of density are described which are segmental or of lobar magnitude or may involve an entire lung. Hilar adenopathy does not appear to be a sign, and cavitation is unusual. The picture changes progressively but slowly as a rule.

Paul and Ritchie[2] agree that roentgenographic features fall into the two general types mentioned above. Paul and Juhl[7] point out that if the case is seen early the lesion is limited to one lung. They

*From the Department of Radiology and Pathology-Oncology, University of Kansas School of Medicine.

**Trainee, National Cancer Institute.

†Gibson, reporting a series of 120 autopsied cases of carcinoma of lung from the University of Kansas Medical Center, described one case which had previously been diagnosed adenocarcinoma which he felt could be included in this group of tumors.

describe the most common shadow as a homogeneous increase in density occupying less than a single lobe. The size of such an opacity varies considerably and the boundaries are ill-defined. It is said to simulate a patch of pneumonic infiltration. They state further that atelectasis is not a feature but in a few instances cavitation is noted. In cases coming to autopsy, involvement of lung tissue has been found in areas where disease was not roentgenographically detectable.

King and Carroll[6] state that the disease is usually extensive and involves a considerable part of both lungs when the patient first comes for examination. They also, however, describe two types of roentgen patterns as outlined above. They stress the importance of serial roentgen examinations and state that roentgen findings on a single film are not characteristic and therefore not diagnostic. Good et al[3] describe the radiographic features in about the same terms as the other authors cited.

Pathology

Two distinct morphologic types of alveolar cell carcinoma are known to exist. The first, described originally in 1876 by Malassez,[8] is diffusely nodular in form and is the more common of the two. The second, described by Musser[9] in 1903, constitutes the diffuse form which may often be lobar in distribution or affect the entire lung and may closely resemble the stage of gray hepatization of lobar pneumonia. This is the rarer type.

It was felt justified to report this case in the literature since it fulfilled the original criteria set down by Cassili and White[10] and later much simplified by Swan[11] for diagnosis of alveolar cell carcinoma.

1. No primary tumor could be found elsewhere in the body.
2. No primary tumor could be demonstrated in the bronchial tree.
3. The tumor must be multicentric with areas of uninvolved parenchyma separating the malignant nodules.
4. The neoplastic cellular process must be confined to the alveolar spaces.
5. The interstitial framework of the lungs, except for lymphatic vessels, must be generally free of the process.
6. The anatomy and histology of the nodules must be unlike any other primary lung process.

Swan condensed this into three major premises.

1. Proliferation of mucous secreting high columnar cells lining the alveoli.
2. Absence of a primary lung tumor in any principal bronchus.
3. Absence of a possible primary cancer focus in the rest of the body.

Case Presentation

This 64-year-old white male was admitted to the University of Kansas Medical Center on August 6, 1951, and expired 13 days following admission. His chief complaint had been dyspnea of three weeks duration with orthopnea, chronic cough, and hemoptysis of about two weeks duration. These symptoms were associated with progressive weakness and fatigability for about two months prior to admission, at which time he noticed a slight fatigability which became progressively worse. At approximately this time he also noted anorexia, headache, and malaise. For two weeks he had been coughing up pink-tinged sputum. He had also noted tightening or constricting sensations across his upper chest. One week prior to admission to the hospital he noted several episodes of well circumscribed pain just to the right of the sternum in the second and third interspaces.

Physical examination revealed a well developed, well nourished white male appearing to be approximately the stated age. The pupils were round and equal and reacted to light and accommodation. Extra-ocular muscles showed physiological responses. Fundi were poorly visualized. The thyroid was not palpable nor were neck masses felt. Chest inspection revealed the excursions to be shallow but equal bilaterally. Rhonchi and moist rales were heard on both inspiration and expiration on the right side posteriorly. An area of dullness to percussion was noted over the right middle lobe. The heart was negative. Blood pressure was 130/85. The abdomen revealed nothing unusual. Genitalia were not remarkable. A one-plus pitting edema was noted in both feet and ankles.

Laboratory findings: urinalysis revealed an acid reaction, specific gravity of 1.024, albumin present as a trace, and sugar slightly positive. There were 9 to 10 pus cells per high power field. A red blood cell count showed 4,780,000, Hb 77 per cent (12 grams), a white blood count of 9,000 and a differential of 77 polys, 22 lymphs, one monocyte and one nucleated red cell per 100 white cells. Serology was negative. NPN was 47 mgm. per cent, creatinine was 1.5 mgm. per cent, sugar was 80 mgm. per cent, Na was 146 meq., potassium 4.6 meq., carbon dioxide combining power was 24.4 meq., serum chloride was 102 meq., cholesterol 195 mgm. per cent with 57 per cent esters. NPN on August 11 was 33 mgm. per cent, sodium 134 meq., potassium 4.7 meq., serum chloride 89 meq. On August 14, 1951, the CO_2 combining power was 26.1. Total proteins were 5.88, albumin 3.91, globulin 1.89. Acid phosphatase .55 units, alkaline phosphatase 1.0 milli mol. units.

Tuberculin, histoplasmin, blastomycin and coccidioidin skin tests were all negative. Routine ag-

glutinations including typhoid O and H, paratyphoid A and B and Brucella were negative. Blood cultures were negative. Sedimentation rate was 20 mm. in one hour. Bone marrow examination was reported as normal marrow tissue. Electrocardiogram revealed sinus tachycardia with a rate of 140, T waves were considered to be at the upper limits of normal in size, consistent with auricular dilatation and hypertrophy.

X-ray of the chest revealed a widespread infiltrative process. The Radiology Department at this time suggested the radiological resemblance between the chest film on this patient (Figure 1) and numerous

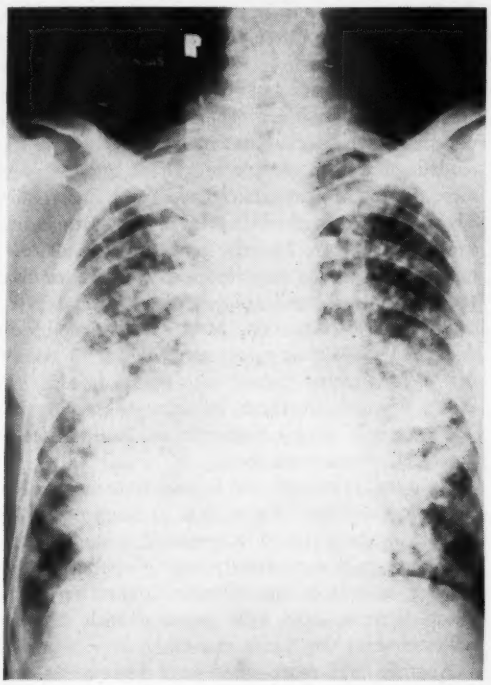


Figure 1. X-ray film. Routine chest film on admission showing diffuse nodular involvement bilaterally with areas of consolidation.

chest films published in the literature illustrating alveolar cell carcinoma and/or pulmonary adenomatosis. Appropriate x-rays failed to reveal evidence of a primary neoplasm in either the gastro-intestinal or genito-urinary tract. Examination of the sputum with the Papanicolaou technic revealed atypical cells, felt to be definitely carcinoma (Figure 2). Hospital course was that of progressive decline with death occurring on August 19 after extreme respiratory distress had been noted for some time.

Anatomical Findings

The body was autopsied approximately three hours postmortem. Examination of the body revealed a male of approximately the stated age in fair

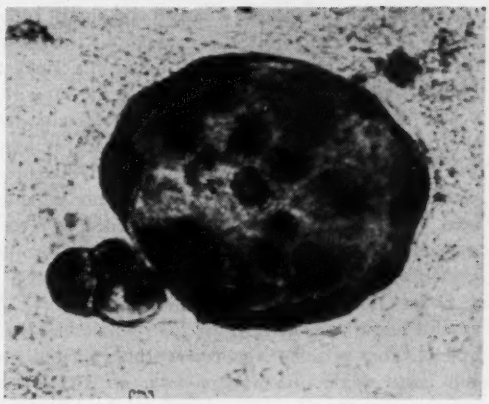


Figure 2. Sputum cytology. Note "characteristic" multinucleated giant cell form. To the left are three cells, one of which shows beginning signet ring formation.

nutrition, approximately 5 feet 11 inches in height and weighing about 170 pounds. Superficial examination revealed a four-plus pitting edema of the lower extremities and a rather deep cyanosis of the face, upper part of the thorax, nail beds and lips. The right pupil was two times greater in size than the left pupil.

Examination of the thoracic cavity presented several interesting findings. Approximately 1000 cc. of straw colored fluid was present in the right pleural space and an equal amount in the left. The pleural surfaces were mottled and both lungs were voluminous and entirely filled the pleural cavities. The lungs were grossly involved by tumor nodules varying in size from a few millimeters up to one-two cm. in diameter. A tendency for coalescence was noted. These nodules were visible through a slightly opalescent pleura. The visceral pleura showed focal thickening and adhesive tabs over the apices of both lungs. The peribronchial and para-

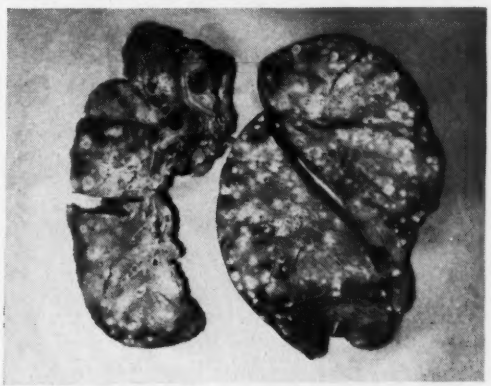


Figure 3. Lung, cut surface. Note widespread miliary-like nodules in left lung. Paratracheal and peribronchial lymph nodes in the right lung. Large node at upper portion of specimen is a paratracheal node.

tracheal lymph nodes were enlarged and almost completely replaced by tumor tissue (Figure 3). Careful dissection of main stem bronchi and the smaller branches outward to the periphery of the lung revealed no intrinsic bronchial lesion to account for the tumor masses in the lung parenchyma. Often, intervening lung tissue without tumor involvement was noted. The pulmonary vessels were not remarkable. The remainder of the autopsy failed to reveal a primary neoplasm which might account for the presence of multiple bilateral pulmonary nodules.

Other gross findings were non-contributory. A careful search was made in the gastro-intestinal tract and in other possible sites for a primary neoplasm, but none was found. There were no nodules or tumor masses noted in the area of the thyroid gland. This gland was not removed, however. A head examination was not permitted. No other metastatic lesions were found in any organ except hilar and paratracheal lymph nodes. The anatomical diagnosis at the time of autopsy was alveolar cell carcinoma of lung with metastases to hilar and paratracheal lymph nodes.

Technic

The bronchi were dissected very carefully peripheralward to a point where the scissor tips could no longer enter a lumen. Following this, numerous sagittal and coronal sections of the entire lung were made at one and two cm. intervals. Any nodules seen to involve a small bronchus were sectioned. No evidence of bronchiolar origin of this tumor was found. Periodic acid, Schiff, and Best's mucicarmine stains were applied to several sections in an attempt to demonstrate mucin production. Reticulum stains were done also to demonstrate the relationship of tumor to stroma (Wilder technique).

Histological Pathology

The microscopic studies revealed a striking picture (Figure 4) entirely different from that seen in the usual bronchogenic carcinomas. The lesion was composed of numerous small nodules containing somewhat distended alveoli which were lined predominantly by a tall columnar epithelium. Frequently cuboidal epithelium was noted, and often this was several cell layers thick. This epithelium was non-ciliated. Often a rather marked tendency to papillary formations was seen. The cell cytoplasm was abundant and eosinophilic. The cell borders were well defined. The nuclei generally were vesicular, ovoid, sometimes irregular in outline and tended to be basically placed. Often nucleoli were seen. Hyperchromatic nuclei were not uncommon. There was no marked degree of intracytoplasmic vacuole formation. Periodic acid, Schiff, and Best's mucicarmine stains together with positive controls revealed only a small amount of intra- and extracellular mucin formation. Most of the alveoli were distended and almost completely filled with sloughing, desquamating tumor cells lying free in the lumen. It was in these instances that numerous "characteristic" signet ring cells and multinucleated giant cell forms were seen.

Only occasional mitotic figures were noted. Nuclear pleomorphism was evident in many cases. No stromal desmoplasia of importance was seen, and the tumor cells were usually resting upon very thin delicate strands of interalveolar connective tissue. Many of these septa were ruptured with resultant coalescence of the tumor masses.

Another and more interesting feature was the

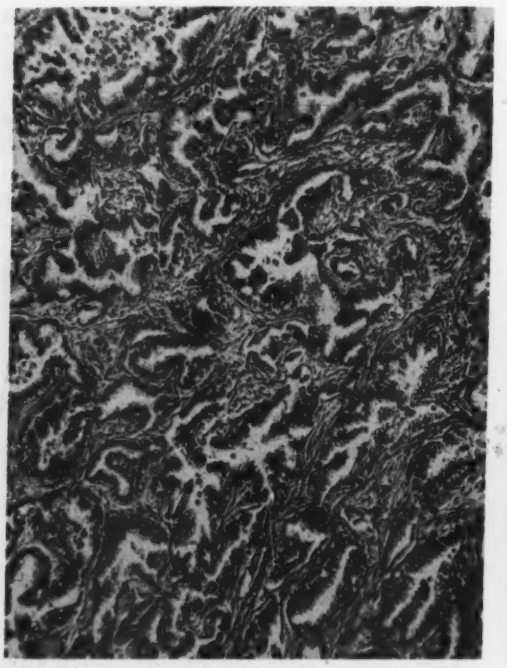


Figure 4. Low power. Note typical adenomatous pattern with papillary formation and alveoli lined by tall columnar cells. Note alveolus at top left filled with desquamating tumor cells.

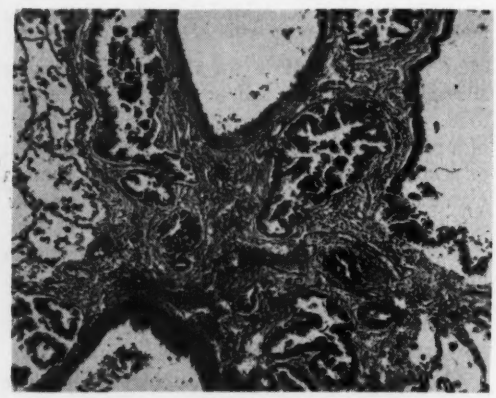


Figure 5. Low power. Note normal bronchus to right and normal lung tissue to the left. Massive lymphatic invasion in perivascular channels by tumor cells.

massive perivascular lymphatic involvement (Figure 5). Constantly, nests of tumor cells were noted in the lymphatic channels particularly along the pulmonary arteries. The hilar and paratracheal lymph nodes showed complete architectural destruction and replacement by tumor with marked desmoplasia. This tumor tissue had taken on a considerable degree of anaplasia.

Stromal inflammation was minimal.

No microscopic evidence was found of metastatic lesions in other organs.

Discussion

Few investigators will deny that alveolar cell tumors exist as a clinico-pathologic entity with definite morphologic patterns. We feel that a rather definite clinical pattern is present. However, this is not the important controversial point. The controversy revolves around the purely academic question of the histogenesis of these tumors. It is not within the realm of this paper to enter into a detailed discussion of this point since this is merely a case report. However, we feel that a brief recapitulation of the arguments is necessary.

Many authors contend that all primary carcinomas of the lung are bronchial in origin. For example, Fried,[12] Herbut[13, 14] and Ikeda[15] feel that all lung cancer is bronchial in origin and arises from small totipotential basal cells beneath the ciliated epithelium which then stream out into the stroma. Others, among them Miller,[16] feel that there is a continuous epithelial lining in the alveoli from which these tumors arise. This view is supported by observations on lungs in cases of bronchiectasis, tuberculosis or any chronic pulmonary infection. Herein, one may see with regularity remarkable epithelial cell proliferation very similar to that seen in so called alveolar cell carcinoma. The majority of people today hold with Miller's views.

Another new and interesting finding was recently reported by Gepts[17] in Belgium in studying an autopsied case. Careful study revealed what he described to be structural bronchiolar abnormalities in the form of small diverticula lined by mucus secreting columnar cells. He feels that this could explain the multicentric origin of this tumor on the basis of the observation that malignancy is commonly seen in embryonic abnormalities. However it is difficult to visualize many bronchiolar diverticula scattered throughout the lung. As was shown by Maximow and Bloom,[18] a few alveoli bud off from the sides of the respiratory bronchioles opposite that along which the branch of the pulmonary artery runs.

Further, as was pointed out by Smith, Knudtson and Watson,[4] and Knudtson and Watson,[5] the lymphatic spread along vessels is rather striking, and they suggest that the multiple nodules found in both lungs may well represent intrapulmonic metastases via the lymphatics, implying, perhaps, that there may be an original, single primary site of origin and that the lymphatic spread may be so rapid as to give the picture suggesting multicentric origin.

The subject of the relationship of this lesion herein described to the so-called pulmonary adenomatosis of sheep or Jaagsiekte was purposely omitted since there are many fine discussions of this in the literature; also, the similarity of this lesion to many chemically induced tumors of lung in the guinea pig and the mouse is not discussed. We feel that there may be a benign lesion (so called pulmonary adenomatosis) in man and that alveolar cell carcinoma is the end stage. Possibly this accounts for some of the successful surgical resections reported by Watson and Smith.[5]

Summary

1. We have reported a case of what is variously described in the literature as pulmonary adenomatosis, terminal bronchiolar or alveolar cell carcinoma. The present case appears to be similar to previously reported cases in all important respects.

2. We have attempted to emphasize the importance of adequate clinical, radiological and cytological examinations.

3. The morphology and histogenesis of this disease process is discussed briefly.

References

1. Weir, A. B., Jr.: Pulmonary Adenomatosis, Arch. Int. Med., 85:806-818, (May) 1950.
2. Paul, L. W., and Ritchie, G.: Pulmonary Adenomatosis, Radiology 47:334-343 (Oct.) 1946.
3. Good, C. Allen, McDonald, J. R., Clagett, O. T., and Griffith, E. R.: Am. J. Roentgenol. and Rad. Ther. 64:1-18 (July) 1950. Alveolar cell tumors of the lung.
4. Smith, R. R., Knudtson, K. P., and Watson, W. L.: Terminal Bronchiolar or "Alveolar Cell" Cancer of the Lung. A report of 20 cases. Cancer 2:977-989, 1949.
5. Watson, W. L., and Smith, R. R.: Terminal Bronchiolar or "Alveolar Cell" Cancer of the Lung. Report of 33 cases. J.A.M.A. 147:7 (Sept. 1) 1951.
6. King, J. C., and Carroll, David S.: Pulmonary Adenomatosis, Radiology: 669-680 (Nov.) 1950.
7. Paul, L. W., and Juhl, John H.: Pulmonary Adenomatosis: Further Roentgen Observations, Radiology 55:681-691 (Nov.) 1950.
8. Malassez, L.: Examen histologique d' un cas de cancer encephaloide du pounon (epithelioma), Arch. de physiol. Noru. et path. 3:353-372, 1872.
9. Musser, J. H.: Primary Cancer of the Lung, Tr. A. Am. Physicians 18:624-636, 1903.
10. Cassili, A. R., and White, H. J.: Rare Forms of Primary Malignant Lung Tumors, Am. J. Clin. Path. 10:623, 1940.
11. Swan, L. L., Pulmonary Adenomatosis of Man, Arch. Path., 47:517 (June) 1949.
12. Fried, B. M.: Primary Carcinoma of the Lung: A Clinical and Pathological Study. Medicine 10:4,373-508 (Dec.) 1931.
13. Herbut, P. A.: Bronchiolar Origin of "Alveolar Cell Tumor" of Lung. Am. J. Path. 20:911-929, 1944.
14. Herbut, P. A.: "Alveolar Cell Tumor" of the Lung; Further Evidence of its Bronchiolar Origin. Arch. Path. 41:175-184, 1946.
15. Ikeda, K.: Alveolar Cell Carcinoma of Lung. Am. J. Clin. Path. 15:50-63, 1945.
16. Miller, W. S.: The Lung, 2nd Edition, Springfield, Illinois, Chas. C. Thomas, 1947.
17. Gepts, W.: Pulmonary Adenomatosis, Report of a Case Demonstrating Peculiar Histological Changes in Certain Bronchioles. Arch. Path. 52:473-479, 1951.
18. Maximow, A. A., and Bloom, W.: Textbook of Histology. 4th Edition, W. B. Saunders Co., Philadelphia, 1942.

Two Attacks of Endocarditis Caused by Different Microorganisms

Joe L. Stockard, M.D.*

Kansas City, Kansas

Introduction: A recent review of 44 cases of subacute bacterial endocarditis, all of which were proved by blood culture, revealed that with the exception of the case presented below, none had a recurrent infection with any organism other than that causing the original infection. For that reason we feel this case should be reported. It emphasizes the importance of identifying the infecting organism in both the original infection and in each recurrence.

J.M., age 52, was first seen with symptoms of cardiac disease in July, 1947. He entered the hospital on that occasion with the complaint of a slow pulse of 24 hours duration. On five previous admissions the patient had shown no cardiovascular abnormalities. An electrocardiogram in February, 1947, had revealed only slight prolongation of the QRS complexes. The rate on this tracing was 88 per minute.

Past History: He had had a migratory arthritis in 1933. The patient's history of this illness was characteristic of acute rheumatic fever. Otherwise the past history was essentially negative.

Physical examination on this admission revealed temperature 98.6° F., pulse 48 and regular, blood pressure 145/70, height five feet nine inches, weight 190 pounds. Examination of the head and neck was negative. Cardiac dullness was not increased. No thrills were felt, but the heart sounds were distant, A2 being very faint. A harsh grade III systolic murmur was heard over the entire precordium but was loudest at the apex. The chest was clear to auscultation and percussion. Except for moderate obesity, the remainder of the physical examination was negative.

Laboratory findings: Rbc. 4,400,000; Hb. 13 gms; Wbc. 8,150; polys. 63 per cent, lymphs 29 per cent. Urine: negative. The electrocardiograms at this time showed a sinus bradycardia with a rate of 48 and a first degree A-V block, the P-R interval being 0.28 seconds.

The patient had no signs or symptoms of heart failure at this time and was dismissed from the hospital without medications. He remained in good physical condition until March, 1948, when moderate dyspnea developed. Examination at that time revealed a harsh grade III systolic aortic murmur and numerous premature contractions. An EKG revealed a rate of 60, frequent premature ventricular contractions, and complete A-V dissociation.

Re-examination in April revealed aortic systolic and diastolic murmurs. The bradycardia and prematurities persisted.

In July, 1950, the patient first noted a low grade afternoon fever. He thought little about this until the latter part of September when, following an upper respiratory infection, the fever increased to a daily elevation of 101-102° F. and was associated with chills and night sweats. He was admitted to the University of Kansas Hospital in November, 1950. Dyspnea was marked at this time.

Physical examination revealed temperature of 100.8° F., pulse 80, blood pressure 140/70, weight 174½ pounds, height 68½ inches. The head and neck were negative. The lungs were clear to auscultation and percussion. The heart was slightly enlarged to the left on percussion. Auscultation revealed grade III aortic systolic and diastolic murmurs. These had remained essentially unchanged. An occasional premature contraction was noted. The patient had a typical Corrigan pulse. No splinter hemorrhages or Osler's nodes were present.

Laboratory findings: Rbc. 3,580,000; Hb. 10.6 gms; Wbc 11,650; polys. 77 per cent; lymphs 19 per cent, eosin three per cent, mono three per cent. Urinalysis: reaction acid; sp. gr. 1.011; heavy trace of albumin; sugar negative; microscopic showed numerous hyaline and granular casts, pus and red blood cells per low power field. Serology was negative. NPN 29 mgm. per cent, creat. 1.2 mgm. per cent, sugar 87 mgm. per cent. The EKG at this time revealed a first degree A-V block with a P-R interval of 0.32 seconds. The rate was 79. During the first four days of hospitalization 10 positive blood cultures were obtained. The organism was a *Streptococcus mitis.* It was found to be sensitive to 0.005 u penicillin/cc.

Hospital Course: On November 9, 1950, he was started on aqueous penicillin, 125,000 units every six hours. He became afebrile on the first day of therapy and remained afebrile thereafter. He showed considerable symptomatic improvement. The dyspnea became much less marked. No change was noted

*From the Department of Internal Medicine, University of Kansas School of Medicine.

in the heart murmur during this period of therapy. Twenty-five subsequent blood cultures were negative. After 60 days of penicillin therapy, he was dismissed.

Following this dismissal he remained asymptomatic for six months. He again developed marked exertional dyspnea in June, 1951. About one month prior to re-admission he first noted paroxysmal nocturnal dyspnea. Digitalization failed to alleviate these symptoms and the patient was admitted to the University of Kansas Hospital on September 10, 1951.

Physical examination on this occasion revealed blood pressure 190/50, pulse 52 and regular, temperature 100.8° F., respiration 24, weight 179, height 68¾ inches. The patient was markedly dyspneic. The head and neck were essentially negative. Percussion of the chest was negative, but auscultation revealed moist rales throughout both lower lobes. The size of the heart was unchanged. The intensity of the aortic diastolic murmur was increased. The abdomen was negative. There was one-plus pitting edema of the ankles.

Laboratory findings: Rbc. 3,820,000; Hb. 11.1 gms.; Wbc 7,550, polys. 69 per cent, lymph 20 per cent, eosin three per cent, mono eight per cent. Urinalysis: reaction acid; sp. gr. 1.018; alb. three plus, sugar negative; Microscopic showed an occasional hyaline cast, 2-4 plus, 4-6 rbc's/hpf. Serology was again negative. NPN 60 mgm. per cent, creat. 2.3 mgm per cent, sugar 100 mgm. per cent. The EKG at this time revealed a rate of 60, frequent ventricular premature contractions, and A-V dissociation. Blood cultures on September 10, 11, and 12 were positive for a hemolytic staphylococcus aureus. This organism was sensitive to streptomycin and chloromycetin. It was resistant to penicillin, aureomycin and terramycin.

Hospital Course: It was our initial impression that this patient had a recurrence of the *Streptococcus mitis* subacute bacterial endocarditis associated with moderately severe cardiac decompensation. On September 15, 1951, he was started on aqueous penicillin 125,000 u every six hours. No symptomatic improvement was noted. Additional therapy included a low salt one to four Gm. sodium chloride daily 1200 caloric diet, aminophyllin suppositories, and digitora gr. 1.28 daily. When we found that the organism on this occasion was a hemolytic *Staphylococcus aureus,* the pencillin was increased to 300,000 u every three hours, and streptomycin 1.0 gm. b.i.d. the first day and 0.5 gm. b.i.d. thereafter was added to the regimen. The digitalis was discontinued. On this therapy symptomatic improvement was rapid, the patient feeling much improved within 72 hours. This therapy was continued from September 22, 1951, until his dismissal October 18, 1951. During this period his chest had cleared completely. His weight dropped from 179 pounds on admission to 150 pounds on dismissal. His last EKG taken on September 21, 1951, showed a first degree A-V block with a P-R interval of .29 seconds. The rate was 75. No premature contractions were present.

Discussion: In the pre-antibiotic era, the mortality associated with the initial attack of subacute bacterial endocarditis was nearly 100 per cent.[1] With the advent of the sulfonamides this dropped to approximately 98 per cent.[2] In Major's[3] series, 15 patients were treated with sulfonamides. Of these 26.6 per cent recovered. Still greater improvement in therapy was noted when, with penicillin, the mortality dropped to 25 per cent. Adequate time has not yet passed for evaluation of the newer drugs and the synergistic actions now available. Obviously these therapeutic triumphs have done away with the greatest difficulty in the treatment of this disease.

However, this therapeutic success creates new problems. These fall into the following general categories: (1) Residual valvular damage leading to congestive heart failure, (2) Inadequate initial therapy resulting in recurrence and increased resistance of the organism, (3) Recurrence due to an entirely different organism.

The patient presented above represents an example of the third situation. His initial infection with *Streptococcus mitis,* most benign of the *Streptococcus viridans* group, was easily cured with relatively small doses of penicillin. The recurrence of the infection with a hemolytic *Staphylococcus aureus* presented quite a different therapeutic problem. This organism was resistant to penicillin but was sensitive to streptomycin. On a combination of penicillin and streptomycin, the blood stream became sterile and has remained sterile to the present time. Had it been assumed that the recurrence was due to *Streptococcus mitis,* the outcome probably would have been very different.

It therefore is important in the treatment of this disease to isolate the infecting organisms with each attack of subacute bacterial endocarditis.

Friedberg[4] mentions one case of subacute bacterial endocarditis in which the infecting organism was different in each of three attacks. All three infections were successfully treated. Wollack and Pomerantz[5] describe a case in which the initial infection was due to a *Stapholococcus aureus* but three recurrences were due to a diphtheroid. The latter were successfully treated with penicillin and bacitracin.

Of some interest is the changing character of

this patient's A-V conduction. One can only speculate regarding the onset. This may well have been due to a recurrence of the rheumatic state. However, the dramatic change which occurred following the treatment of the recurrent infection led us to believe that at that time the infection itself was a contributory cause. The last EKG taken on January 7, 1952, shows a P-R interval of 0.22 seconds. Improvement in A-V conduction during treatment of subacute bacterial endocarditis has been noted by Friedberg.[6] He states that it occurs in approximately 15 per cent of the cases of subacute bacterial endocarditis.

Conclusions

1. Recurrence of subacute bacterial endocarditis may be due to different organisms.

2. The organisms should be identified in each attack of subacute bacterial endocarditis.

I wish to express my appreciation to Dr. Ralph Major for his assistance in the preparation of this report.

Bibliography

1. Seaburg, John H.: Arch. Int. Med. 79:1, 1947. Subacute Bacterial Endocarditis, Experiences in the Past Decade.

2. Libman, E., and Friedberg, C. K.: Subacute Bacterial Endocarditis: New York, Oxford University Press. 1948 2nd edition.

3. Myers and McKinley: The Chest and the Heart Vol. II: Thomas Co., Springfield, Ill. Page 1630.

4. Friedberg, C. K.: W. B. Saunders Co., Philadelphia and London, 1949, page 777.

5. Wollack, R., and Pomerantz, N.: A.M.A., Arch. Int. Med. 88:840. Combined Antibiotic Therapy: Report of a Case of Subacute Bacterial Endocarditis Reinfected with a Diphtheroid and Successfully Treated with Penicillin and Bacitracin.

6. Friedberg, C. K.: Diseases of the Heart, W. B. Saunders, Philadelphia and London, 1949, page 789.

Intravenous Avertin: A Preliminary Report

Roger W. Bumgarner, M.D., Richard L. Pokorny, M.D., Ernst T. Morch, M.D., and Paul H. Lorhan, M.D.*

Kansas City, Kansas

Tribromethyl alcohol or avertin was first reported in 1923 by Willstätter and Duisberg[1] of Germany. Eichholtz[2] recognized its anesthetic properties in 1927 and administered it rectally for anesthesia. The following year rectal avertin became very popular in Germany and in 1929 "avertin fluid" was marketed for rectal use and universally accepted.

The Council on Pharmacy and Chemistry of the American Medical Association accepted avertin as a basal anesthetic in 1937.[3] They stated that more than 700 references on avertin had appeared in the literature and the majority were favorable regarding its use as a basal anesthetic agent. It was felt that the toxic effects observed in the early clinical reports were due to overdosage and poor knowledge of the contraindications.

Avertin intravenously was first used by Kirschner[4, 5] of Germany in 1929. He used a three per cent concentration in saline and later in a five per cent solution of calarose. He administered a predetermined dose calculated from body weight and reported on 750 cases with a three per cent incidence of venous thrombosis. Freinstein[6] used a three per cent solution of intravenous avertin in 570 cases. Avertin was the sole agent for 180 minor cases, and for the remainder it was used as induction to ether anesthesia. Martens[7] frequently observed cyanosis and venous thrombosis in a series of 310 cases. Niemann[8] gave 250 intravenous avertin anesthesias, nine of which were for Cesarean sections, and in all cases the child was depressed. Thornton and Rowbotham,[9] while with a maxillo-facial surgical unit of the British Army during World War II, used one per cent avertin in five per cent dextrose. They preferred its use to pentothal sodium especially when intubation was necessary, because of a lesser incidence of laryngospasm. Furthermore, avertin patients could be intubated earlier when the larynx had been previously cocanized. Evans[10] states, "In the case of avertin the period of recovery is very frequently further complicated by great restlessness, such as requires two people to keep the patient in bed." For this reason, plus the respiratory depression, "it found no permanent place as an intravenous anesthetic."

Chemistry and Pharmacology

Avertin is a white crystalline powder with a melting point of 80° C. The structural formula is that of ethyl alcohol with three bromine atoms substituted on one of the carbon ($CBr_3 CH_2 OH$) atoms. Aqueous solutions are prone to decompose, forming hydrobromic acid and dibromacetaldehyde. Contrary to other investigators, Parsons [11] found that avertin does not decompose readily when exposed to light and air at room temperature, having kept solutions under those conditions for as long as three months without evidence of decomposition. However, he recommends mixing the solution just prior to use. It is marketed under the name of "Avertin with Amylene Hydrate" as a solution of

*From Department of Anesthesiology, University of Kansas Medical Center, Kansas City, Kansas.

tribromethanol with one gram of tribromethanol and 0.5 gram amylene hydrate in one cc. of the solution.

Sollman[12] stated that amylene hydrate renders avertin more soluble but also modifies its action, in itself being a narcotic, by increasing the depth and duration of anesthesia, and is additive to respiratory depression. Barlow and Duncan[13] are of the opinion that amylene hydrate contributed little to the narcosis but somewhat more to the respiratory depression.

Conflicting statements concerning the pharmacological physiology are found in the literature. The pertinent facts are as follows:

1. Narcotic effects: Avertin depresses the diencephalon and its action also extends to cortical centers.[12]

2. Respiration: In full anesthetic doses, rectal avertin depresses the respiration and respiratory arrest is prone to occur. When used in "proper doses" is rarely causes respiratory depression. Avertin produces marked relaxation of the jaw muscles and the airway is easily obstructed. This must be guarded against.[14]

Using rectal avertin, Wood[15] reported "the respiratory center may frequently be affected, the respirations may decrease in number but usually are slightly increased and become shallow in excursion."

3. Circulation: With rectal avertin there is an early, transient fall in blood pressure averaging about 25 mm. mercury. Occasionally, as in hypertension, the systolic pressure may drop as much as 100 mm. mercury. This lowered blood pressure lasts for 5-15 minutes and is rarely dangerous. The hypotension is thought to be due to the depressant action of avertin on the medullary vasomotor centers, as well as some degree of direct action on the heart and blood vessels. Avertin further sensitized the heart to epinephrine irregularities.[12] The coronary arteries are dilated, the force weakened and rate slowed with resulting cardiac dilatation and fall in blood pressure.[11]

4. Gastro-intestinal: The motility of the gastrointestinal tract is markedly depressed by doses of avertin having a slight hypnotic action.[16]

5. Genito-urinary: Due to the fall in blood pressure, urinary output is decreased for as long as two hours following avertin administration. Urea output is decreased. Hemorrhagic nephritis and albuminuria are occasionally seen.[12] Kirschner,[5] using three per cent avertin normal saline intravenously, observed hematuria in a few cases but saw no hematuria when he changed to a three per cent solution in five per cent dextrose. Pitt[17] stated, "In spite of the conditions which tend to hamper renal function during anesthesia, nitrogen excretion is actually very little upset by the volatile anesthetics and less so by avertin." Renal insufficiency lowers considerably the margin of safety of the drugs.[14]

6. Liver: It is generally agreed that avertin has little effect on the normal liver. One to two per cent show slight impairment of liver function and occasionally a severe hepatitis results.[12]

7. Metabolic: The temperature usually falls, blood sugar is elevated slightly and there is some decrease in the alkali reserve.[12]

8. Relaxation: Muscular relaxation varies with the dose given, being only partial in light anesthesia and marked with doses which produce deep surgical anesthesia. If cyclopropane or ether in small amounts is used as a supplement to a basal anesthetic dose of avertin, adequate relaxation can be obtained.[14]

9. Central nervous system: Avertin lowers the intracranial and intraocular pressure. Most observers feel that this is an advantage in neurosurgery; however, Wood[15] is of the opinion that it should not be used in brain surgery because of its effect on the respiratory center.

10. Detoxification: There are diverse opinions regarding the detoxification of avertin. It is frequently stated that avertin is combined with glucuronic acid in the liver and its detoxification is therefore slowed with impaired hepatic function. However, it has been shown[18] that the liver plays no important role in the coupling of avertin with glucuronic acid. The avertin was coupled and detoxified in the normal time even when the liver was destroyed by ethylenchlorhydrin. It has also been found that an animal starved for several days shows delayed detoxification. This was not a result of low glucose or insulin content, as one or both of these substances do not affect the detoxification.

Avertin is excreted by way of the kidneys, mainly as avertin glucuronate. The bromine remains in the organic molecule and is not ordinarily excreted as the ion.[12] Anschutz[18] reported that excretion begins in 45 minutes, maximum is reached after four hours and in 24 hours most is excreted. Only traces are found after this. Welsch[19] found that 69 per cent was excreted during the first 24 hours and 29 per cent in the next 24 hours.

Analgesia, in the sense of indifference to pain, is present when the patient recovers partial consciousness, and is able to appreciate sensations. After regaining consciousness, patients fall into a quiet but easily rousable sleep lasting several hours.[12]

Preparation for Intravenous Use

Avertin solution, one per cent, as used intravenously is prepared by adding five grams of tribromethanol (five cc. of avertin) to 500 cc. of five per cent dextrose in distilled water. The dextrose solution is first warmed in a water bath to approx-

imately 40° C. Avertin is then added and the mixture shaken vigorously until the avertin dissolves and the solution clears. Avertin will go into solution in the aqueous dextrose at room temperature if it is slowly added (one to two cc. at a time) and shaken vigorously. This requires about three to five minutes. The solution is tested with congo red before administration and used only if the color is pink. It is recommended that the solution be freshly prepared and not used after it has been standing.

Method of Administration

Avertin is administered by the Murphy drip technique, so that between 75 and 150 cc. may be given rapidly (30-90 seconds). Venepuncture is made with an 18-gauge needle. Avertin can be administered rapidly until the desired stage of anesthesia is attained, then the drip is stopped until the patient shows signs of lightening. Then an additional amount of avertin is given rapidly. Following the suggestion of Dr. Brian McGurk,[20] we have been administering the induction dose rapidly, then slowing and adjusting the rate of flow to keep the patient at the desired level of anesthesia; this method, we feel, is more satisfactory.

Summary of Cases

This is a preliminary report of 50 cases in which avertin was used intravenously in a one per cent concentration in five per cent dextrose in distilled water. Avertin was the sole anesthetic agent in 11 cases. Nitrous oxide was used as a supplement in 13 cases. Avertin was used as a secondary agent in the remaining 25 cases. Curare was administered in those cases requiring further muscular relaxation.

Intubation was performed in over 50 per cent of the cases with avertin being selected because intubation was contemplated.

In the series there were 28 males ranging in age from two to 80 years, and 22 females ranging from 18 to 83 years. The duration of anesthesia ranged from 30 minutes to over seven hours. The majority of the cases were for endoscopies although various other surgical procedures were performed, i.e. head and neck, intrathoracic, intra-abdominal, perineal and orthopedic operations.

No serious postoperative complications were noted. Two patients had a mild thrombosis in the veins used for administration. One death occurred in the series. This was a valvulotomy, the patient dying of a pulmonary embolus on the 10th postoperative day.

Discussion

From this small series of cases using avertin intravenously and a review of the literature, we feel that this drug shows promise and that reinvestigation, both experimentally and clinically, is indicated.

In a perusal of the literature, we have found many discrepancies, disagreements and misquotations regarding the pharmacology of avertin. Most of the experimental work was carried out within the first five years following its introduction. As far as we can ascertain, nothing new has been added to the literature since 1935. Many of the investigations have never been confirmed. Clinical studies were postulated on small series, with avertin being given in predetermined doses by the rectal route. Of the several reports of intravenous avertin, all but Thornton and Rowbotham[9] administered precalculated doses according to body weight.

Avertin intravenously was not widely accepted because of its difficulty of preparation, instability in solution, the thromboses it caused, the use of predetermined doses which undoubtedly caused excessive depression, unfamiliarity with endotracheal anesthesia and postoperative excitement.

The one per cent solution is not too difficult to prepare. We have kept it for a period of three weeks without evidence of deterioration as shown by the congo red test. The two cases of thrombosis, in our opinion, were not severe enough to contraindicate its use. In our hands, the continuous Murphy drip technique gives considerable latitude and we have seen no severe depression of respiration or circulation. Contrary to Evans'[10] statement on excitement in the immediate recovery period, our patients have had a quiet serene recovery. The patients seem to have a longer period of analgesia and amnesia than with other agents. Following diagnostic bronchoscopies, the nurses in our recovery suite have pointed out that patients cough much less and it is not the spasmodic type seen following the pentothal-curare technique.

Intravenous avertin was selected because intubation was contemplated. We found, as did Thornton and Rowbotham,[9] that patients can be intubated more safely in lighter planes of anesthesia than with pentothal. With the application of local anesthesia to the base of the tongue and larynx, some have been intubated while responding to vocal commands.

Conclusions

We feel that intravenous avertin will find a place in the armamentarium of the anesthesiologist. It may be indicated in operations on the head and neck, endoscopies, and intubations. Its value in operations requiring muscular relaxation, in neurosurgery, perineal, and orthopedic procedures and in any long operations will have to be determined by trial. Toxicity should carefully be re-investigated. Contraindications must be scientifically determined.

Bibliography

1. Willstater, R., and Duisberg, W.: Bir. duetsch. Chem. Gesellock. 56:2283, 1923.
2. Eichholtz, E.: Deutsche med. Wchnschr. 53:710, 1927.

3. Avertin: Report of Council on Pharmacy and Chemistry. J.A.M.A. 109:952, Sept. 18, 1937.
4. Kirschner, M.: Eine psycheschonende und steuerbore Form der Allgemein-betäubung. Chirurg: 1:673, June 15, 1929.
5. Kirschner, M.: Erfahrungen mit der intravenösern Avertinnarkose. Arch. f. klin. Chir., 162:361.
6. Freinstein, Waldemar: Die intravenöse Avertinnarkose nach. Kirschner. Klin. Wchnschr. 9:742, April 19, 1930.
7. Martens, E.: Erfahrungen über die Anivendung der intravenöse Avertin-infusion nach Kirschner. Zentralbl. fur Chirurgie 58:I; 524, 1931.
8. Niemann, G.: Intravenoser Avertinnausch bei Gynakologischon Eingriffen. Zentrabbl. fur. Gynakologic. 54:III 2826, 1930.
9. Thornton, H. L., and Rowbotham, S.: Anesthesia in a Maxillo-facial Surgical Unit with the British Liberation Army. Anesthesiology 6:580, Nov. 1945.
10. Evans, F. T.: Modern Practice in Anesthesia. Hoeber, New York, 1949, p. 307.
11. Parsons, F. B.: Some Pharmacological Aspects of Avertin. Brit. M.J. II, 709, 1929.
12. Sollman, Torald: A Manual of Pharmacology. W. B. Saunders. Philadelphia, 1948, p. 667-9.
13. Barlow, O. W., and Duncan, J. T.: The Influence of Morphine on the Premedication Tribromethol (avertin) and Tribromethanol fluid (Avertin Fluid) in Relation to Nitrous Oxide Anesthesia. J. Pharmacol. and Exper. Therap. 49:50, 1933.
14. Goodman, L., and Gelman, A.: The Pharmacological Basis of Therapeutics. The Macmillan Co., New York, 1941, p. 100-101.
15. Wood, Dorothy: Tribromethanol as a Preoperative Narcotic. Calif. and Western Med. 33:719, 1930.
16. Quigley, J. P., Barlow, O. W., and Himmelsbach, C. K.: Correlation of Visceral and Somatic Activity Following Administration of Hypnotics. A. Barbital Compounds and B. Tribromethal. C. Avertin Fluid and Crystals. J. Pharmacol. and Exper. Therap. 49:50, 1933.
17. Pitt, N. E.: The Influence of Avertin Upon the Renal Function. Lancet I:741, March 30, 1935.
18. Anschutz, W.: Zur Frage der Rauschnarkose mil Avertin. Zentralbl. fur. Chir. 57:1500, June 14, 1930.
19. Welsch, A.: Cehmische Untersuchungen zur Avertin frage. Arch fur Experimentalle Path. und Pharm. 139:302, 1929.
20. McGurk, B.: Personal Communication.

A Method for the Rectal Use of Nisulfazole in Chronic Ulcerative Colitis*

William R. Durkee, M.D.**

Manhattan, Kansas

Since the introduction of the sulfonamides, various ones have been tried in the therapy of chronic nonspecific ulcerative colitis. In 1941, Weber et al.[1] mentioned that 2-(p-nitrobenzenesulfonamido)-pyridine might have therapeutic application in the treatment of lower intestinal infections. Later a similar compound, 2-(p-nitrobenzenesulfonamido)-thiazol, was produced and studied. When it was found[2] that both these compounds were not readily absorbed from the intestinal tract, their effects on patients suffering from ulcerative colitis were investigated. In the first report of the clinical use of these compounds in ulcerative colitis,[2] five cases were treated with encouraging results. For purposes of simplification, 2-(p-nitrobenzenesulfonamido)-pyridine has been designated Nisulfadine, and 2-(p-nitrobenzenesulfonamido)-thiazol has been designated Nisulfazole.

Although both compounds were used in the early cases, it was found that Nisulfadine frequently caused nausea. Therefore, its use was abandoned. Nisulfazole has produced few toxic effects and can be continued for long periods of time. In the early cases, Nisulfazole was administered only by mouth. A 0.3 gram tablet containing 50 milligrams ascorbic acid was used and given initially in doses of four to six grams daily. Nisulfazole, when administered by mouth, is partially converted into sulfathiazole in the intestinal tract, and both compounds appear in the blood. Later, a 10 per cent suspension of Nisulfazole in pectin was developed for administration by rectum. There was practically no absorption of the compound when given rectally, and this mode of administration was equally effective in controlling the disease process. The suspension has been ordinarily given in doses of 30 cc. twice daily, sometimes diluted with 30 to 60 cc. of water.

As is well known, the results of any treatment of nonspecific ulcerative colitis are difficult to evaluate because of the tendency to spontaneous remissions and relapses. However, the results of the use of Nisulfazole have been encouraging. In 1948, Major[3] reported on the use of Nisulfazole in 40 cases over a period of six years. He reported recovery in 33 and improvement in seven. The term "recovery" was employed when the patient was symptom free and the x-ray picture showed a normal colon. "Improvement" was used to designate patients who had no diarrhea and normal stools, but whose roentgenograms of the colon were not normal. Eleven of the patients had relapses which were again controlled by Nisulfazole. Most of Major's patients received the medication both by mouth and by rectum.

Wills reported on the use of Nisulfazole in 24 cases of ulcerative colitis.[4] Fifteen of the 24 patients showed definite improvement with this medication. Of the nine without improvement, four were in the polypoid hyperplastic stage. Wills used the rectal suspension exclusively if the x-ray showed involvement of the rectum and the lower colon only. The suspension was combined with oral tablets in doses of four to six grams daily if the x-ray showed more extensive involvement of the colon.

The use of the 10 per cent suspension in pectin by rectal instillation has come to be the more accepted method of using Nisulfazole because of the

*From the Department of Medicine, University of Kansas School of Medicine, Kansas City, Kansas.
**Now with the Ball Memorial Clinic, Manhattan, Kansas.

absence of nausea and because of the small amount of the compound which is absorbed systemically. The usual procedure in this clinic has been to administer 30 cc. of the suspension, containing 3.0 grams of Nisulfazole, usually mixed with 30 cc. of water, through a soft rubber catheter into the rectum. During this procedure, the hips of the patient are elevated and remain so for 20 to 30 minutes. Although this method has been helpful in a large number of cases, recently some doubt has arisen concerning the height which the suspension reaches in the colon. Wills[4] watched the progress of the suspension through the sigmoidoscope and reported that within a few minutes it had spread above the range of the sigmoidoscope and evenly coated the mucosal surfaces for observed periods up to two to six hours without redosage in some cases.

We undertook a study using a mixture of the Nisulfazole suspension with barium and examining the patient roentgenographically at varying time intervals. The suspension was given to five patients in the usual manner—in 60 to 90 cc. quantities with the hips elevated. It was given to one patient who assumed the knee-chest position for three minutes after the instillation, and to another who assumed the knee-chest position for five minues, then lay on his right side for 10 minutes. None of these patients had ulcerative colitis. It was found that the highest point of penetration up to six hours later was the sigmoid colon in three (43 per cent) and some portion of the descending colon in four (57 per cent). There was no penetration past the splenic flexure.

Because of the poor results using a small volume of solution, it was decided to use 400 to 500 cc. of a barium suspension containing 30 cc. of the Nisulfazole suspension, given slowly over a one- to two-hour period with the patient lying on his back. The procedure was well tolerated by most patients, only two being unable to retain this volume. In a series of 43 procedures, five of which were on three patients with ulcerative colitis, the results were as follows:

Solution reaching the ascending colon, 18 (42%)

Solution reaching only as high as the transverse colon, 11 (25%)

Solution reaching only as high as the descending colon, 9 (21%)

Solution reaching only as high as the rectosigmoid colon, 3 (7%)

Solution not retained, 2 (5%).

Of the five procedures done on patients with ulcerative colitis, two showed barium in the ascending colon, one in the descending colon, and two in the rectosigmoid colon. Although the series was too small to be significant, it was our impression that there was little difference in the height to which the suspension went between those patients with ulcerative colitis and those with illnesses unrelated to the colon. Early in the study it was found that the barium would appear higher in the colon if the roentgenogram was obtained two hours after the completion of the instillation than if the x-ray picture was taken immediately after the instillation was completed. In no patients were there any ill effects from the Nisulfazole or the procedure.

Although further trial and experience are necessary, it is suggested by this study that, when using Nisulfazole by rectal instillation in the treatment of chronic nonspecific ulcerative colitis, it can best be given as 30 cc. of the suspension in pectin mixed with 400 to 500 cc. of water. This mixture is given by a slow drip per rectum over a one- to two-hour period, followed by a further period of two hours of inactivity and rest in bed. This method would obviate the necessity of giving Nisulfazole by mouth in those cases of ulcerative colitis which show lesions radiographically extending into the ascending colon. It is also suggested by this study that whenever a medication is given by rectum for its effect locally on the colon, it is best given slowly in a large volume.

It is a pleasure to thank Dr. Ralph H. Major for his suggestions and encouragement in the course of this investigation.

Bibliography

1. Weber, C. J., Lalich, J. J., and Major, R. H. Reduction of 2-(p-Nitrobenzenesulfonamido)-Pyridine to Sulfapyridine in the Animal Body. Proc. Soc. Exp. Bio. and Med. 48:616, 1941.
2. Major, R. H., and Douglas, H. L. The Treatment of Ulcerative Colitis with Nisulfadine and Nisulfazole. J. Kansas Med. Soc. 1942.
3. Major, R. H. Nisulfazole in the Treatment of Chronic Ulcerative Colitis. Stanford Med. Bulletin 6:147, 1948.
4. Wills, C. B. The Use of Nisulfazole in the Treatment of Ulcerative Colitis. Rocky Mt. M.J. 46:743, 1949.

93rd Annual Session

KANSAS MEDICAL SOCIETY

Kansas City, Kansas April 27-May 1, 1952

Hemorrhagic Transfusion Reactions

Charles H. McCroskey, M.D.,* and Stanley R. Friesen, M.D.*

Kansas City, Kansas

The ready availability of blood for multiple transfusions in surgical practice has resulted in better preoperative preparation of patients, the safer accomplishment of extensive surgery and a more rapid rehabilitation of seriously ill patients. Because of the widely prevalent use of blood in recent years, the absolute incidence of transfusion reactions has increased. Because of newer and improved technics in blood-matching, the relative incidence has probably decreased in proportion to the number of transfusions given.

Not the least serious of the types of transfusion reactions which may develop after the infusion of incompatible blood is the development of a marked hemorrhagic tendency. This occurrence may result in serious bleeding and may be the only indication that an anesthetized patient is undergoing a transfusion reaction.

Attention has been directed to the problem of massive generalized wound bleeding during operation in a previous report of seven cases.[1] The bleeding was observed as an "ooze" of dark blood from all cut surfaces which was virtually refractory to the usual methods of hemostasis. Uncontrollable exsanguination resulted in death in five of these cases.

Careful analysis of these cases strongly indicated that the transfusion of incompatible blood was probably the sole causative factor for the abnormal bleeding. That a hemolytic reaction had taken place was apparent. It was felt that other possible etiological factors such as shock, anesthetic agents and drug sensitiveness were not responsible for the hemorrhagic state. There was a discouraging lack of response to measures used in attempt to control the bleeding, such as intravenous calcium, vitamin K, fresh blood given directly or indirectly, anti-hemophiliac globulin, topical and intravenous thrombin, intravenous procaine, anti-histaminics, protamine sulfate and toluidine blue, and, in some, splenectomy. However, the protamine sulfate and toluidine blue were given in dosages considered now to be insignificant and inadequate.

Although the evidence seemed to incriminate transfusion reactions as the basis for the hemorrhagic state, positive evidence of mismatching in the ABO system was demonstrable in only one case. Utilization of more recent tests for the detection of incompatibility in the Rh system might have prevented some of the disastrous hemorrhagic transfusion reactions described above.

To understand the mechanism of any type of reactions resulting from incompatible transfusions, a brief review of the basic concepts involved is advisable. The red blood cells of every human being contain many different blood group substances which are divided into nine systems. The antigens in each of these systems are inherited independently of the antigens in each of the other systems.[2] The individual blood-group antigens vary in their ability to stimulate the production of antibodies. Some antigens, like A, B, and D (Rho) are strong antigens, but only in those individuals who lack them. Others, like O, N, and P are very weak antigens; others are intermediate in antigenicity.[2] The clinical importance of these various blood-group antigens depends on their antigenicity. A person lacking a particular antigen in the red blood cells is susceptible to sensitization by that antigen if exposed to it by transfusion, intramuscular injection, or by transfer of fetal blood across the placenta.

Human blood group antibodies are found in the serum of most human beings in various combinations. Only persons of Group AB are not likely to have naturally-occurring blood-group antibodies of any kind. Since the discovery of the Rh blood groups, not only have a large number of specific blood-group antibodies been discovered but it has also been shown that any one may exist in different forms, such as a "saline-active" form, an "albumin-active" form and a "blocking" form.[2]

The presence of blood-group antibodies other than anti-A and anti-B in any individual implies previous sensitization (isoimmunization) by parenteral injection or by placental transfer of the antigen. An indication of the likelihood of encountering naturally-occurring as well as induced blood-group antibodies is seen by the fact that anti-A, anti-B, anti-C (Rh') and anti-D (Rho) are found simultaneously in a fair number of women who are Group 0, Rh-negative. In one carefully examined serum from a repeatedly transfused patient, nine different specific blood-group antibodies were found simultaneously.[2]

Transfusion of incompatible blood results in agglutination and hemolysis of the donor's cells by the serum of the recipient—an antigen-antibody reaction. Practically speaking, this more commonly is a result of mismatching with the antigens A, B, and

*Department of Surgery, University of Kansas School of Medicine, Kansas City, Kansas.

D (Rho). However, at least a dozen of the lesser blood group antigens are sufficiently antigenic to sensitize some recipients who lack them. If sensitization does occur, reactions to future transfusions are likely. Fortunately, actual sensitization is not likely to occur frequently because of the low antigenicity of these lesser blood group substances.[2]

That marked hemorrhage may ensue in hemolytic transfusion reactions is confirmed by isolated reports in the literature.[3, 4, 5] In an extensive study on the immunological aspects of transfusion reactions, Brown[6] has demonstrated a consistent blood clotting defect, the nature of which has not been reported. He has noted this clotting defect also in dogs undergoing hemolytic transfusion reactions.

Other evidence that hemorrhagic disorders may result from blood group incompatibilities is seen in the hemolytic type of erythroblastosis fetalis. These babies may have abnormal bleeding.[7] The production of anaphylactic shock in dogs after sensitization with a suitable antigen is well known to render the blood incoagulable. An increased amount of circulating heparin and the activation of fibrinolysin have been demonstrated in this condition.[8]

A group of patients experiencing transfusion reactions from incompatible blood more recently has been studied by the authors.[9] It was apparent from these studies that the hemorrhagic state may develop as a result of the infusion of blood incompatible in either the ABO or Rh systems. Furthermore, for the hemorrhagic diathesis to occur it was noted that the reaction was usually of a hemolytic type in which 250 cc. of blood or more had been given. The administration of such amounts of incompatible blood is possible in an anesthetized patient in whom the usual signs of a reaction are masked.

Although the exact nature of the clotting defect is not known, these studies demonstrated that there may be an increased amount of heparin-like substance (as measured by the Allen protamine titration test[10]) circulating in the blood and that increased fibrinolytic activity, which results in the dissolution of fibrin clots, attends the reaction. Hemolysis itself is probably not the cause of the hemorrhagic state.[11] Moreover, the use of toluidine blue dye (15 mgm. per kilogram body weight in one liter of isotonic fluid intravenously) adequately controlled the abnormal bleeding as well as brought about a reversion of the abnormal heparin levels and fibrinolysis to normal.

Similar findings of a hemorrhagic state in hemolytic transfusion reactions have been reported by Muirhead.[12] He has also found increased levels of heparin-like substances which responded to toluidine blue therapy.

Although the hemorrhagic state resulting from incompatible transfusion is uncommon, the possibility of its occurrence must be emphasized. It behooves every physician who contemplates transfusing patients with blood to take certain precautions concerning the selection of both the blood and the patient. Every patient who is to be transfused should be carefully questioned for a history of previous transfusions or previous transfusion reactions. If the patient is a woman additional information regarding pregnancies and hemorrhagic disturbances should be obtained. It is generally agreed that husbands (or their immediate relatives) should not be used as donors for their wives unless an emergency exists and other donors are not available.

Avoidable human errors in the selection of blood probably account for a majority of incompatible transfusion reactions; consequently extreme care in the typing and cross-matching of blood is necessary. The routine employment of the indirect Coombs test[13] would provide greater safety by the detection of unsuspected Rh antibodies in previously sensitized patients. It should be remembered that sensitization by one or more blood group antigens is possible whenever transfusions are given.

References

1. Friesen, S. R., and Nelson, R. M.: The Occurrence of Massive Generalized Wound Bleeding During Operation With Reference to the Possible Role of Blood Transfusions in its Etiology; Am. Surg., 17:609-622, 1951.

2. Soutter, L., Allen, F. H., Jr., and Emerson, C. P.: Blood Grouping, Blood Banking, and Blood Transfusion; N.E.J.M., 245: 367-375, 410-424, 456-464, 1951.

3. Weiner, A. S.: Blood Groups and Transfusions; Charles C. Thomas, Springfield, Ill., 1943.

4. Levine, E. C., and Segall, H. N.: Post-transfusion Reactions, Alterations in Blood after Ether Anesthesia and After Blood Transfusions; Surg. Gyn. and Obs., 35:313, 1922.

5. Lattes, L., (1932) in Whitby, L. E. H., and Britton, C. J. C.: Disorders of the Blood; Blakiston Co., Phila., 1946, p. 535.

6. Brown, I. W., Jr.: The Immunological Aspects of Transfusion Reactions. Presented to the Society of University Surgeons, Feb. 1951. Personal communication to one of the authors.

7. Potter, E. L.: Rh, Its Relation to Congenital Hemolytic Disease and to Intragroup Transfusion Reactions; The Yearbook Publishers, Inc., Chicago, Ill., 1947.

8. Rocha e Silva, M.: The Role Played by Leucocytes and Platelets in Anaphylactic and Peptone Shock; Ann. N.Y. Acad. Sciences, 50:1045-1063, 1950.

9. Friesen, S. R., Harsha, W. N., and McCroskey, C. H.: Massive Generalized Wound Bleeding During Operation With Clinical and Experimental Evidence of Blood Transfusion Reactions. Reported before the A.M.A., Atlantic City, June 13, 1951. To be published.

10. Allen, J. G., Moulder, P. V., et al.: A Protamine Titration As an Indicator of a Clotting Defect in Certain Hemorrhagic States; J. Lab. & Clin. Med., 34:473-476, 1949.

11. Authors' experimental observations.

12. Muirhead, E. E.: Incompatible Blood Transfusions With Emphasis on Acute Renal Failure; Surg., Gyn. & Obs., 92:734-746, 1951.

13. Coombs, R. R. A., Mourant, A. E., and Race, R. R.: A New Test for the Detection of Weak and "Incomplete" Rh Agglutinnins; Brit. J. Exp. Path., 26:255-266, 1945.

BLUE SHIELD

Public Relations Potential

It has been said that good public relations is 95 per cent good service and five per cent interpretation—interpretation being the job of convincing the public that you do have good service.

Blue Shield and Blue Cross Plans throughout the country are becoming increasingly aware of the tremendous value of identifying themselves with doctors and hospitals. This identification if thoroughly performed would have the effect of convincing the public that the non-profit prepayment plans are in a state of active cooperation with those who actually produce the service—that is the doctors and the hospitals.

There is an intriguing chain of thought in connection with more public relations for Blue Shield through participating physicians. For example there are 1,500 Blue Shield participating physicians. It is quite likely that each one of these physicians has an average of at least 10 patients visiting his office six days a week. If Blue Shield could have an attractively designed poster which might be changed each month hanging on the wall in each participating physician's office, this poster would be seen by at least 15,000 people a day. Not only would it succeed in getting across an important message about Blue Shield but it would further serve to solidify the impression in the public mind that Blue Shield is in fact sponsored and backed by the medical profession.

The big problem in an undertaking of this kind is not the preparation of the message—it is the simple little job of getting the poster up on the doctor's wall.

In the past Blue Shield has distributed information cards through physicians' offices and there has been considerable response from these cards. However, there is a much greater potential in the poster approach. This subject will be presented to the physicians on the Blue Shield Relations Committee during the coming months.

Blue Shield and Blue Cross are temporarily suffering from the high standard they have maintained in the product they are offering to the people of Kansas. A small percentage of people tend to seek cheaper contracts which often times fail miserably when people are hospitalized or need physician service. The job ahead of us now is to demonstrate to the people the need for the program which maintains a high standard of protection first and then the fact that Blue Cross and Blue Shield are maintaining this standard. The public still does not thoroughly understand what has happened to hospital costs in the past few years. Few people realize that hospital bills can amount to $1,000, $1,500 and even $3,000. That is why some people are attracted to prepayment plans of commercial insurance companies which promise certain cash indemnities at lower rates than Blue Cross and Blue Shield have to charge. Because of the lack of awareness of the real problem in hospital costs, these policies seem reasonably adequate to the uninitiated.

The Blue Cross and Blue Shield Plans in Kansas are trying to make use of every medium possible for getting this story across to the public. However, newspaper and radio advertising are costly. It would take many thousands of dollars to carry out such a campaign to the extent that the public might really get the message. This is why the Kansas plans are beginning to turn to physicians and hospitals to win their support in carrying this important story to the people of our state.

Report on Research

In the last few days members of the Kansas Medical Society have received a pamphlet entitled "A Report on Research," published by the University of Kansas School of Medicine with the request that these be placed in the physicians' waiting rooms.

The pamphlet, on enameled paper, presents the over-all picture of the different diseases and conditions upon which research is conducted at the school, cancer, heart disease, high blood pressure, poliomyelitis, newborn baby deaths, sterility, and arteriosclerosis. The engravings used as illustrations were made from photographs taken by students.

The Journal calls attention to this publication in the hope that all physicians will comply with the request that the pamphlets be placed in waiting rooms. Contributions for the support of the research program are welcomed by the school, and the knowledge conveyed in the booklet may prompt donations to continue the research.

Better health and higher standards of living are among the most potent weapons in the fight against Communism in Southeast Asia and Japan, two top executives of Parke, Davis and Company declared recently at the conclusion of a 25,000-mile business trip. Harry J. Loynd, president of the firm, and W. R. Jeeves, director of overseas operations, who talked to prominent government officials and businessmen everywhere they went, said they had encountered a "growing awareness of the importance of better health and everything that contributes to it. . . If any of those governments turn to Communism, it will be by force of arms, not by voluntary means."

PRESIDENT'S PAGE

Dear Doctor:

I would like to remind each of us who are now and have been trying to practice an ethical and a high type of medicine to survey and take inventory of the assets we have accumulated from the deficit our alma mater experienced the day we were graduated. I am of the opinion that we will see that we have obviously benefitted greatly and that we owe our school a little more than gratitude.

The American Medical Association is a co-partner in an educational foundation, and has this past year contributed $500,000 to the medical schools of this country; 1800 doctors subscribed an average of $55 each, while the layman interested in medicine and our well being subscribed much more than we did, which, in my humble opinion, is contrary to the laws of self preservation.

The American Medical Education Foundation is a permanent organization, and it is hoped that each physician can see fit to make some annual contribution. The amount you give is to be determined by only one person; that person is, of course, YOURSELF. This amount is construed by the foundation and the specific school you designate as a symbol of your interest in keeping the schools going and not as a debt you owe. The donation is tax free. I am too embarrassed to put into print the number of Kansas physicians who last year participated, but I feel that when we call attention to the workings of this very fine organization and the high ideals for which it stands we shall, as we always do, rally to the cause and demonstrate to our respective schools, to the foundation and all interested lay organizations that we are still interested in the future of medicine. Your central office will handle your checks and will answer any questions that you might have that concern the entire program.

The weather was most extravagant with disappointments and embarrassments on March 3, 1952. If there is anyone who doubts this statement, I refer you to Acting Dean Hashinger and Mr. Oliver Ebel.

The committee selected to make a complete study of the Social Welfare Board's health care problems as they concern the client, the hospital, the druggist and the doctor is making headway, and at the House of Delegates meeting a report will be made, even though it will not be complete.

O. A. Benage

EDITORIAL COMMENT

Sixth Annual University Issue

The Journal is proud to present the Sixth Annual University of Kansas School of Medicine issue. It will be noted that the scientific contributions are original papers prepared by the faculty at the medical school. The occasion also provides an opportunity to discuss the achievements of the school and the cooperative spirit existing between the medical profession of this state and the university.

The long list of achievements is all the more remarkable for the fact that they have been accomplished within the past few years. The school has grown in size since 1949 when the Kansas legislature appropriated some four million dollars for additional buildings and equipment. This expansion, currently nearing completion, has erected upon the site of the medical center a veritable educational and hospital city.

A larger enrollment now enables more Kansas young men and women to study medicine. One hundred five instead of the previous 80 students are currently being enrolled in each class. The preceptor program has become a reality within the past few years and is already demonstrating its effectiveness. Students obtain direct knowledge of the actual practice of medicine, and the practicing physician is benefitted by having a student work with him.

One of the great accomplishments is the addition of color television to the teaching curriculum. This, now included in several departments, is in daily use and makes the University of Kansas School of Medicine the first institution of its kind to use the new teaching method.

Graduate education has progressed dramatically. This continually expanding project is attracting not only increasing numbers of Kansas physicians but also doctors from all over the United States. More courses and expanded enrollments have been experienced each year since the program began.

The above is in no way a tabulation of the achievements at our school of medicine. It represents, rather, a comment on only a few of a great many that could be recorded. Among the others should be a story on research, expanded effort in lay education, and many more.

The Kansas Medical Society is proud of this school and is taking a large interest in its progress. This year finds such interest and cooperation more apparent than ever before. The future is promising. The Kansas Medical Society and the medical school will combine their efforts toward the creating of an institution of learning that will be outstanding among all in the United States. They will continue to jointly sponsor every worthwhile effort toward the end that the people of Kansas may have the finest possible health service and medical care. All this has already been achieved in large measure, but the accomplishments of the past create additional challenge for the future, which provides an opportunity for even greater achievements for the years ahead.

Kansas Medical Day

The Fourth Annual Kansas Medical Day was held in the University of Kansas Medical Center, Kansas City, on Monday, March 3. It is the one day of the year during which the junior and senior students of the medical school are guests of the Kansas Medical Society.

The 1952 program was exceptional because of a different type of program than conducted during the past similar occasions. The purpose of this is to create an interest in these young men and women in practicing medicine in Kansas. During past years, various physicians from different parts of the state have spoken on subjects relating to their work, their recreation, and their communities.

This year the program was presented by outstanding business and professional men of Kansas. The theme was taken from the Declaration of Independence through the use of the words, "Life, Liberty, and the Pursuit of Happiness."

The morning session was devoted to "Life," or more specifically, "Life in Kansas." Mr. Maurice E. Fager, director of the Kansas Industrial Development Commission, Topeka, spoke on Kansas industry. Kansas manufacturing was covered by Mr. Fred Stein, president of the Stein Laboratories, Atchison, and past president of the Kansas State Chamber of Commerce. Kansas aircraft was discussed by Mr. Robert Chatley, public relations director of the Cessna Aircraft Company, Wichita. Kansas finance was discussed by Mr. Claude Pack, president, Home State Bank, Kansas City, and past president of the Kansas Division of the American Bankers' Association.

The afternoon session dealt with "Liberty," during which time the four freedoms were the titles of the presentations. Freedom from want was spoken upon by Ray I. Throckmorton, dean of the School of Agriculture, Kansas State College, Manhattan; freedom of speech by Mr. Ed Abels, editor and publisher of the *Lawrence Outlook*, Lawrence; freedom of worship by Dr. Eugene M. Frank, pastor, First Methodist Church, Topeka, and freedom

from fear by Capt. James Flatley, commanding officer of the Naval Air Station, Olathe.

The evening was devoted to "Pursuit of Happiness," with the junior and senior students and their wives or friends as guests of the medical society. Following a social hour, dinner was served at the Town House Hotel, Kansas City, and after a few introductions the remainder of the evening was spent dancing.

American Medical Education Fund

The American Medical Education Fund plans to raise, through voluntary contributions, at least $1,000,000 annually, which fund is to be distributed among the 72 medical schools in the United States. Contributions to this fund are expected to come primarily from the medical profession, both organized societies and individuals.

The background, in its briefest outline, should begin with a story of the National Fund for Medical Education. This, headed by Mr. Herbert Hoover, consists largely of lay persons and organizations who are interested in medical education. They are appealing to individuals for donations for medical schools. The American Medical Education Foundation is supported by the American Medical Association and may be considered as the medical portion of the national fund. The national fund has a goal of five million dollars, of which one million is the responsibility of the medical profession. Last year the American Medical Association gave a half million dollars. All other medical contributions for the year totalled less than $250,000.

The money is disbursed to the schools under three classifications. The first is a grant of equal size to each approved medical school in the United States. The second is an additional grant based on a uniform annual sum per student enrolled in each approved medical school in the United States. The third represents special grants to individual schools on the basis of particular needs or problems. This last named category can become of significance only when the fund is of considerably larger size than at present. Last year, for instance, each medical school received $15,000 under the first category and $17 per student under the second, or an average of about $5,600. It is hoped that in future years some four million dollars will be distributed through the first two grants and that additional funds will be available for grants of the third type.

The Journal of the American Medical Association has repeatedly carried information on this program, but in spite of continual effort physician contributions have been discouraging. A few months ago it was written into the Congressional Record by Senator James E. Murray, during a debate on the Federal Aid to Medical Education bill, that "I am glad that the AMA is urging members every week to individually contribute a hundred dollars a year to the support of our medical schools. But I am sorry to note that during the first 24 weeks of that campaign less than three one-hundredths of one per cent of the country's physicians was in sufficient agreement with the AMA's position to make such an individual contribution. . . . When you add up the list of those who did, you will find that it represents approximately .003; three one-hundredths of one per cent of the doctors of America agree with the AMA's leadership as to how that which the AMA itself calls 'A Challenge to the Medical Profession' should be met."

The aims and objectives of the American Medical Education Foundation are familiar to everyone concerned. The remaining problem is merely to create sufficient interest so that a large portion of our practicing physicians will make a contribution. Checks should be mailed directly to the American Medical Education Foundation of the American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois. Amounts of any denomination are acceptable, and special emphasis is made to acquaint each physician with the fact that contributions may be earmarked for specific schools. These will be sent to those schools, and individual credit for the contribution will be received. The entire project is voluntary, but the ultimatum is whether enough physicians will support the voluntary program to remove the current attempt to bring this into a compulsory level and under bureaucratic control. Senate Bill 337 is still before the Congress. If this voluntary program succeeds, it will remove the need for federal aid. Should federal aid be granted, medical education under private enterprise will have been lost.

Annual Meeting, April 27-May 1

Plans for the 93rd annual meeting of the Kansas Medical Society are rapidly being completed. The session will run from April 27 through May 1, in Kansas City, Kansas, with members of the Wyandotte County Medical Society as hosts.

The first item scheduled on the program is a meeting of the Board of Directors of Kansas Physicians' Service (Blue Shield), to be held on Sunday, April 27. On the following day there will be the usual sports events, a golf tournament and a skeet shoot, with a tournament banquet in the evening.

Scientific sessions at the Memorial Auditorium will begin on Tuesday morning, April 29, and will continue there until Thursday noon, May 1. The

afternoon on Thursday will be devoted to a clinical program at the University of Kansas Medical Center, covering many of the newer phases of chronic rheumatic heart disease.

Two meetings of the House of Delegates will be held during the session, both at the Town House, Kansas City's new hotel. The first will be a dinner meeting on Tuesday evening and the second will be a luncheon meeting on Thursday noon. All new business to be considered at the 1952 session should be presented at the first meeting as the introduction of new business at the second session requires the consent of two-thirds of the voting delegates present.

Some component societies have not been represented at former meetings of the House of Delegates, and each group is urged this year to send its maximum number of delegates to each session. The House of Delegates, primary legislative and governing body of the Society, is composed of officers, councilors, and past presidents of the Society and one delegate for each 20 members or major fraction thereof of component societies.

The following well known speakers have accepted invitations to take part in the scientific program:

Maurice E. Davis, M.D., Associate Professor, Obstetrics and Gynecology, University of Chicago—Obstetrics and Gynecology.

L. Kraeer Ferguson, M.D., Professor of Surgery, Graduate School of Medicine, University of Pennsylvania, Philadelphia—Surgery.

Thomas Findley, M.D., Professor of Clinical Medicine, Tulane University, New Orleans—Medicine.

H. F. Fraser, M.D., United States Public Health Service Hospital, Lexington, Kentucky—Drug Addiction.

George J. Garceau, M.D., Professor of Orthopedic Surgery, University of Indiana, Indianapolis—Orthopedics.

C. Allen Good, M.D., Associate Professor of Radiology, Mayo Foundation, Graduate School, University of Minnesota—Radiology.

Bayard T. Horton, M.D., Associate Professor of Internal Medicine, Graduate School, University of Minnesota—Medicine.

Phillip J. Howard, M.D., Department of Pediatrics, Henry Ford Hospital, Detroit—Pediatrics.

James B. McNaught, M.D., Head of Department of Pathology, University of Colorado School of Medicine and Hospitals—Pathology.

R. D. Pruitt, M.D., Assistant Professor of Medicine, Graduate School, University of Minnesota—Medicine.

Alfred Sugg, M.D., Ada, Oklahoma—Urology.

Owen H. Wangensteen, M.D., Professor of Surgery, University of Minnesota—Surgery.

General chairman for the meeting is Dr. Lee H. Leger. Other committee chairmen are as follows: Scientific Program, Dr. William H. Algie; EENT Scientific Program, Dr. Clifford J. Mullen; Commercial Exhibits, Dr. Peter E. Hiebert; Scientific Exhibits, Dr. Hughes W. Day; Arrangements and Banquet, Dr. C. Omer West; Publicity, Dr. Oscar W. Davidson; Entertainment, Dr. Michael J. Ryan; Reception, Dr. Glenn R. Peters; Auxiliary, Dr. Leland N. Speer.

Nominations for K.M.S. Offices

The following physicians have been nominated for offices in the Kansas Medical Society, the election to take place on the last day of the annual session to be held in Kansas City, April 27-May 1:

President-elect	L. R. Pyle, M.D., Topeka P. W. Morgan, M.D., Emporia
First vice president	M. C. Eddy, M.D., Hays J. G. Hughbanks, M.D., Independence
Second vice president	H. H. Jones, Sr., M.D., Winfield J. M. Porter, M.D., Concordia
Constitutional secretary	D. D. Vermillion, M.D., Goodland J. D. Colt, Jr., M.D., Manhattan
Treasurer	J. L. Lattimore, M.D., Topeka Dwight Lawson, M.D., Topeka
A.M.A. Delegate (term of 1953-1954)	L. S. Nelson, M.D., Salina T. P. Butcher, M.D., Emporia
A.M.A. Alternate Delegate (term of 1953-1954)	G. F. Gsell, M.D., Wichita C. V. Black, M.D., Pratt

Additional nominations for any office may be made from the floor.

The first step towards prevention of occupational tuberculosis (in hospitals) is to uncover every case of communicable tuberculosis among the patients. That requires chest x-ray examination of every patient on admission. Only when both employees and patients have chest x-rays does the hospital break the vicious cycle: infection of personnel by patients, with no one being aware that these patients have tuberculosis, and infection of patients by the personnel who continue on duty for months before being aware that they themselves are ill with tuberculosis. The prevention of tuberculosis in the personnel is only one of the several reasons for admission chest x-rays. In the interest of the patients, admission chest x-rays should be done even if there were no occupational disease problem.—*Leopold Brahdy, M.D., The Canadian Nurse, November, 1951.*

Case Reports From The University of Kansas Medical Center Tumor Conference*

Bone and Joint Tumors

Edited by R. E. Stowell, M.D., and D. M. Gibson, M.D.**

Case No. 51-109

R. B., a 36-year-old white woman, was admitted to the University of Kansas Medical Center on August 23, 1951, with a chief complaint of pain and swelling of the left knee. She first noticed weakness of the left knee one year prior to admission; there was no history of injury. Two or three months prior to admission she first noticed a small tumor on the left knee, which was enlarging and was accompanied by some tingling and pain. Physical examination revealed a tumor mass one inch in diameter visible on the medial side of the patellar tendon at the joint line. The mass disappeared on flexion of the knee. There was no swelling of the joint. The tumor mass was firm in consistency, was not attached to the skin, and produced some limitation to movement. On August 24, 1951, an arthrotomy of the knee was done and a tumor mass attached to the medial meniscus was removed. The patient's postoperative course was uneventful and she was discharged September 2, 1951, to be followed in the out-patient department.

Dr. Haslam: Geschickter and Copeland[1] found a semilunar tumor mass which measured three cm. in diameter. It was attached to the medial meniscus, and to the synovial tissue by a pedicle. On cut section the tissue was yellowish brown with some lobulation. Microscopically the main tumor mass is lobulated and is composed of dense cellular tissue with numerous large multinucleated giant cells. In some areas there is distinct brown pigment. In one place there is a characteristic xanthomatous area composed of large cells with foamy cytoplasm and small, dense nuclei. This is a benign giant cell tumor.

Dr. Haslam: Geschickter and Copeland[1] found that eight of 17 tumors (excluding osteochondromas or chondromatosis) of joints were giant cell tumors, or xanthomas. Among the preoperative possibilities were lipomas, fibromas, fibrosarcomas and hemangiomas. These were all less frequent in this series than giant cell tumors, or xanthomas. This tumor was easily exposed surgically and the tumor and medial meniscus were removed; there was some synovial membrane adjacent to the cartilage that was removed with the tumor to be sure of adequate excision. This case is typical. The tumor involves the knee joint much more commonly than other joints. De Santo and Wilson[2] in 1939 reported nine cases and found 32 more in the literature up to that time. This tumor usually occurs between the ages of 20 and 40. Thirty-six of the 41 cases were in the knee. There are three types distinguished: pedunculated, multiple and diffuse. Malignant changes have not been reported, but De Santo and Wilson's review[2] reported seven local recurrences following excision. This patient had an uncomplicated convalescence and is back at work.

Dr. Weaver: The figures of Geschickter and Copeland[1] certainly do not correspond with our experience here. In this institution we've had one xanthoma of the knee joint before this one. It had a pedicle arising from synovia, and it was exceedingly simple to remove. We have had some six or seven hemangiomas of the knee joint, which might give similar symptoms. In 1941 I reported[3] several cases of hemangioma of the knee joint and reviewed over 30 cases in the literature. I think the xanthomas are a much rarer tumor than the hemangiomas and some of the other tumors around the knee joint.

Dr. Firminger: Giant cell tumors of bone may become malignant. I agree with Geschickter and Copeland[1] in thinking that irradiation may accelerate or aid in the development of malignancy from giant cell tumors in the bone.

Dr. Helwig: We have in our material at least three or four examples of so-called benign giant cell tumors which destroyed the patient by metastasis. In one case the metastases looked just about as benign cytologically as the primary lesion, although there is usually atypical proliferation of the spindle cell elements.

Case No. 51-108

D. H., a 13-year-old boy, was admitted to the medical center on March 15, 1950, with a chief complaint of swelling of the left knee. The preceding December and January he suffered some pain in the left knee following injuries. The pain sub-

*Cancer teaching activities aided by a grant from the National Cancer Institute and the Kansas Division of the American Cancer Society.

**Postdoctoral clinic research fellow of the Damon Runyon Memorial Fund for Cancer Research.

sided, but he had had some intermittent pain in the following weeks. On March 1 some swelling was noted, accompanied by marked tenderness. X-ray shortly thereafter showed a lesion of the lateral condyle. It was diagnosed as a bone tumor and the patient was referred to this hospital for treatment. Physical examination revealed a moderately tender, definitely warm mass over the lateral aspect of the left knee just above the joint. This mass was firm and appeared fixed to the deep structures. Biopsy of the tumor was performed on March 17, 1950, and on March 22, 1950, a mid-thigh amputation was done. A pressure dressing and mild traction were maintained. The stump healed well, and the patient was dismissed, to be followed as an outpatient.

Dr. Tice: Roentgenograms of the left knee show bone destruction of the lower end of the femur and a little bone production, radiating in the form of a sunburst architecture out from the shaft; it also shows a triangular shadow in the destructive area

Figure 1. Roentgenograms of left femur of patient 51-108 showing altered architecture of osteogenic sarcoma.

that we speak of as Codman's triangle. The roentgenograms are classical of osteogenic sarcoma. Kolodny[4] points out in a rather large series that many osteogenic sarcomas occur around the knee, either at the lower end of the femur or the upper end of the tibia. The bone destruction is the most important thing, and bone production is often present also. In Kolodny's series,[4] 18 per cent of his cases showed a sunburst type of bone production, so that is not necessarily present. I think that the triangular demarcation of the tumor is the most important factor in forming the diagnosis. The outline of the shaft is usually preserved.

Dr. Firminger: The gross specimen consisted of the left leg; in the region of the lateral condyle there was a tumor which extended for about two cm. into the soft tissue and extended into the marrow cavity for about three cm. Microscopically, the tumor is characteristic of osteogenic sarcoma.

Dr. Weaver: From practically every viewpoint this case is classical of osteogenic sarcoma. The age group, the history, the physical findings, location of the tumor, and the x-ray and microscopic picture are all typical. These tumors are most discouraging to treat. Out of 150 cases we have two that have survived over 10 years; one that has lived over five years; one that has lasted three years; and we have several in the one and two-year group. Aside from these few, they are all dead. We don't have much to offer these patients in the way of curative treatment. When we have determined, by biopsy, that we are dealing with an osteogenic sarcoma, we suggest to some responsible member of the family that an amputation be done. They ask, "If we do this, is he going to be all right?" We have to say, "Probably not—the chances are that within one to three years this will metastasize to the lungs and will end fatally." Why should we subject the boy to amputation? It is either this or nothing. X-ray is not the treatment of choice but may sometimes give palliation. If we do an amputation the patient can go ahead without any pain and, for a period of time, lead a fairly normal existence. If amputation is not done, the patient starts taking aspirin, codeine, morphine, until he becomes an addict, and he will come back eventually, begging for amputation. By this time all hope is lost.

This boy gave a history of trauma. The role of trauma in osteogenic sarcoma is difficult to evaluate. Dr. Coley[5] was positive that trauma was an etiological factor. Others are just as positive that it has nothing to do with it. Trauma may aggravate the growth of some tumors.

Dr. Helwig: If trauma were an important factor we would expect to see these tumors frequently in relation to the millions of fractures that occur, yet the occurrence of osteogenic sarcoma in non-pathologic traumatic fracture is practically unknown.

Case No. 51-110

C. C., a 62-year-old man, entered on October 1, 1951, with the chief complaint of soreness in the left leg for six months and swelling of the upper leg for one month. Six months previously he first noted the onset of intermittent dull aching pain in the left hip, associated with slight limitation of straight leg raising. This had progressed so that the patient, due to severe pain, was unable to raise his left leg more than one foot off the bed. One month prior to admission he noted swelling on the outer aspect of the left upper leg near the hip, accompanied by slight pain and soreness. There had been

a 10-pound weight loss in the past four to six months, with some anorexia. The significant physical findings were confined to the extremities. There was a large, smooth, firm mass 10 x 8 cm. in size, with slight tenderness to palpation, located on the lateral aspect of the left leg just below the hip. Active leg raising was limited to 20°; passive leg raising was normal. Laboratory studies were within normal limits. On October 3, 1951, the femoral tumor was biopsied. A short time later the leg was amputated.

Dr. Tice: Roentgenograms of the upper femur show an expansive type of pathological process with widening of the shaft and minimal bone destruction along the lateral aspect. There is soft tissue swelling and some bone production in the soft tissues and along the medial aspect. The shaft has a fibrocystic type of architecture. This picture suggests a malignant bone-producing tumor, an osteogenic sarcoma. Although this is primarily a tumor of youth and adolescence, according to Kolodny,[4] 14 per cent of patients with Paget's disease develop osteogenic sarcoma. We have had one such case in the past and I thought this to be another.

The possibility of a metastatic tumor from the kidney was suggested by the pathologist on the basis of the biopsy. For this reason, retrograde pyelograms were done, which showed a filling defect in the calyces on the right side. It is not possible to exclude this kidney as the source of a malignant process. The bone lesion resembles a primary tumor more than a metastasis on the basis of the expansive type of growth and the bone production. A metastatic growth ordinarily destroys bone.

Dr. Firminger: The biopsy, which shows tissue with a fibrous stroma containing interlacing bundles of undifferentiated cells and areas suggestive of osteoid, was interpreted as being either a metastatic undifferentiated renal cell carcinoma or an osteogenic sarcoma.

The amputated specimen showed thickening of the cortex of the femur over the medial aspect, and thinning of the cortex over the lateral aspect. Anteriorly, the cortex was broken through by a large yellowish mass of tissue that was extending into the muscle. In some areas this tissue was soft, while in other areas it was hard and appeared to contain bony material.

Microscopically, this tumor, the bulk of which is composed of undifferentiated spindle-shaped cells, osteoid and poorly formed spicules of bone, is an osteogenic sarcoma.

Dr. Weaver: It is interesting that Dr. Tice, Dr. Haslam and I independently came to the same conclusion that this was an old Paget's disease with an osteogenic sarcoma superimposed. The idea that it might have been a metastatic renal carcinoma had not entered my mind until the pathologist raised the question. Metastatic renal carcinomas are exceedingly interesting to the orthopedist because we see a great many of them that metastasize to bone. Many times these are huge solitary tumors; the patient often complains of the bone lesion but has no complaint at all relative to his kidneys. Metastatic renal carcinomas in bone are usually bone-destructive lesions. Frequently they are pulsating tumors with a pronounced bruit. If one sees a pulsating tumor that is remote from a major blood vessel, the first thing to consider is a metastatic renal carcinoma.

This tumor was quite vascular, but not nearly so vascular as one expects in a metastatic renal carcinoma. We felt that amputation of this part was indicated, regardless of whether it was metastatic or otherwise. Osteogenic sarcomas in elderly people do occur. We have had three or four in this institution in persons over 70 years of age.

Bibliography

1. Geschickter, C. F., and Copeland, M. M.: Tumors of Bone, 3rd Edition. J. B. Lippincott Co., 1949, Philadelphia, page 698.
2. De Santo, D. A., and Wilson, P. D.: Xanthomatous Tumors of Joints. J. Bone and Joint Surg. 21:531-558, 1939.
3. Weaver, J. B.: Hemangiomata of the Lower Extremities. With Special Reference to Those of the Knee-Joint Capsule and the Phenomenon of Spontaneous Obliteration. J. Bone and Joint Surg. 20:731-749, 1938.
4. Kolodny, A.: Bone Sarcoma. Surgical Publishing Co., 1927, Chicago.
5. Coley, W. B.: Local Injury as a Causative Factor in Bone Sarcoma with Special Reference to the Medico-Legal Aspects. Publications of the Hospital for Ruptured and Crippled. Vol. V.

ACTIVITIES OF MEMBERS

Dr. M. M. Swan, Great Bend, has accepted an appointment as part time physician at the Great Bend annex of the Larned State Hospital.

* * *

Dr. Dan W. Bolton, Frankfort, has been appointed health officer for Marshall County for 1952.

* * *

Dr. Mahlon H. Delp, chairman of the Department of Postgraduate Medical Education at the University of Kansas School of Medicine, was one of the speakers at a regional meeting of the American Hospital Association held in Wichita recently. His subject was "The Function of the University Medical Center in Improving Care in Small Hospitals of the State."

* * *

The Arkansas City Medical and Surgical Clinic announces the addition of three physicians to its staff. Dr. Vernon L. Weeks, formerly of the Veterans Administration Hospital in Des Moines, and Dr. John W. Franklin, who is completing a residency at the University of Iowa Hospital, will specialize in internal medicine. Dr. William W. Kridelbaugh, now of the department of surgery at the

University of Iowa School of Medicine, will specialize in surgery.

* * *

Dr. E. S. Edgerton and Dr. Larry E. Vin Zant, Wichita, were speakers at a recent meeting of the Sedgwick County Chapter of the American Cancer Society.

* * *

Dr. Francis J. Bice, who has been practicing in Wakeeney since the end of World War II, closed his office there last month to go into active service with the Navy. He reported to Memphis, Tennessee, and was commissioned as Lieutenant Senior Grade.

* * *

Dr. A. N. Lemoine, Jr., chairman of the Department of Ophthalmology at the University of Kansas Medical Center, presented a paper, "Choice of Operation in Cataract Surgery," at the Pan-American Congress of Ophthalmology held in Mexico City in January. He also had an exhibit on cataract sutures at the meeting.

* * *

A feature story on Dr. H. L. Stelle, who has practiced in Pittsburg for 46 years, was published in a recent issue of the Pittsburg Headlight.

* * *

The Gelvin-Haughey Clinic, Concordia, announces that Dr. R. A. Chapman is a new member of its staff, specializing in internal medicine. He is a graduate of the University of Illinois School of Medicine, served his internship with the Navy and spent two years in the Navy medical corps. He recently completed a residency at the University of Illinois Hospital, Chicago.

* * *

Dr. Glen E. Martin, who formerly practiced in Paola and Goodland, has moved to Wakeeney and has opened an office there.

* * *

The Ashley Clinic, Chanute, announces that Dr. Don R. Abbuehl, a diplomate of the American Board of Surgery, is now a member of its staff. Dr. Abbuehl is a graduate of the University of Kansas School of Medicine, has had two years service with the Army medical corps, and has received surgical training at the V. A. hospital in Wadsworth.

* * *

Dr. Paul C. Laybourne, Jr., of the University of Kansas Medical Center, was speaker at the annual health education meeting of the Wyandotte County Medical Auxiliary held in Kansas City on February 12. His subject was "Emotions of Living."

* * *

Dr. Paul W. Schafer and Dr. Creighton A. Hardin, of the University of Kansas Medical Center, were speakers at a meeting of the Society of University Surgeons held at Johns Hopkins Hospital last month. They described a method of replacing part of a vital artery.

* * *

Two papers which originally appeared in the Jonurnal of the Kansas Medical Society were condensed in the February issue of Digest of Ophthalmology and Otolaryngology, "Congenital Toxoplasmosis" by Dr. Frances Ann Allen of Newton and "Glomus Jugulare Tumor" by Dr. David M. Gibson and Dr. G. O'Neil Proud of the University of Kansas School of Medicine.

* * *

Dr. Raymond A. Schwegler, Jr., Lawrence, is scheduled to appear as a speaker at the Fifth American Congress on Obstetrics and Gynecology at Cincinnati on April 4. His subject is "Prevention and Treatment of Postpartum Hemorrhage."

* * *

Dr. Louie F. Barney, Kansas City, a past president of the Kansas Medical Society and of the Wyandotte County Medical Society, has announced his retirement after having practiced in Kansas City for 48 years.

* * *

A county-wide celebration in honor of Dr. Lottie F. Law is being planned by clubs in Hill City for March 30. Dr. Law will complete a half century of medical service this spring.

* * *

Dr. George S. Hopkins, Topeka, has been appointed chief surgeon of the Santa Fe Railway, Panhandle and Santa Fe Railway, and the Atchison, Topeka and Santa Fe Hospital Association.

* * *

Dr. E. L. Gann, Emporia, was speaker at a recent meeting of the Outlook Club in that city. He discussed work of an ear, nose and throat specialist and showed a film on surgery for cancer of the larynx.

* * *

Dr. Middleton L. Perry, Topeka, was recently honored by the University of Tennessee Medical School, his alma mater, for nearly 60 years of medical service. An award from the university was presented to Dr. Perry at the February meeting of the Shawnee County Medical Society.

* * *

Dr. Albert C. Hatcher of Wellington and Dr. Karl Menninger of Topeka were recently named to the state advisory committee on adult boarding homes.

* * *

Dr. E. E. Brooks, Burden physician for the past 45 years, was guest of honor at a community celebration held recently. The address of the day was given by Governor Edward F. Arn.

Senior Thesis from the University of Kansas Medical School*

A Comparative Study of Insulins**

Herman W. Hiesterman, M.D.

Kansas City, Missouri

Mechanism of Action of Insulin

Much of the mechanism of the action of insulin is not yet understood. It appears to consist primarily in abolishing the inhibitory effect of an anterior pituitary hormone and other inhibitors on the hexokinase which phosphorylates glucose-6-phosphate, the form in which glucose is metabolized. Insulin exerts its action at more than one site in the huge metabolic pool of chemical equilibrium involving carbohydrate as well as protein and fat.

The blood sugar lowering action which insulin displays is brought about mainly by the following well established effects: (1) withdrawal of glucose from the blood and its deposition as glycogen in the muscles, (2) decrease of hepatic glycogenolysis, and (3) decrease of hepatic gluconeogenesis from non-carbohydrate precursors, namely, fat and protein.

Insulin decreases lipemia and cholesterolemia and prevents deposition of excess fat in the liver. It reduces the level of ketone bodies in the blood to normal, apparently by making unnecessary the excess conversion of fats to glucose. In diabetes it protects the remaining islet cells from exhaustion and subsequent degeneration. The formation of fat from carbohydrate is increased under the influence of insulin.

The serum potassium falls when insulin is administered because of an increased uptake of potassium by the body cells. Similarly, the inorganic phosphate of the blood is lowered as a result of the increased cell intake of phosphorylated hexoses.

Time Activity of Various Insulin Preparations

Five types of insulin have become available for use in diabetic therapy. They are: regular insulin, crystalline insulin, protamine zinc insulin, globin insulin with zinc, and NPH insulin. Each of these has characteristics which give it a definite place in the treatment of diabetes.

Unmodified Insulin: Regular insulin and crystalline insulin represent the hormone in a nearly true state. Regular insulin is a solution of amorphous insulin, whereas crystalline insulin is a solution of zinc insulin crystals. Their rates of action are similar although crystalline insulin is slightly less intense in effect and slightly more prolonged than regular insulin. This difference is insignificant, however, when compared with other modifications of insulin. The only important difference is that crystalline insulin, because of its lower protein content, produces fewer allergic reactions than does regular insulin.

Unmodified insulin is the most prompt in action and least prolonged of all insulin preparations. The characteristic effect of a single subcutaneous dose of unmodified insulin is demonstrable within an hour, reaches its peak in from three to six hours, then quickly subsides and is exhausted in about eight to 12 hours. These values are approximate and apply only to doses within the usual therapeutic range. With larger doses they are greater and with smaller doses they are less. Another factor playing an important role in the effective duration of a dose of insulin is the severity of diabetes. In mild diabetes the return of hyperglycemia is slower during waning insulin action than in severe diabetes. The above values are those seen in diabetes of moderate severity.

Protamine Zinc Insulin: This modification of insulin is a suspension of a relatively insoluble compound of insulin, protamine, and zinc in a buffered vehicle. A subcutaneous dose of this suspension forms a depot which releases insulin slowly so that its action is spread over a longer period of time.

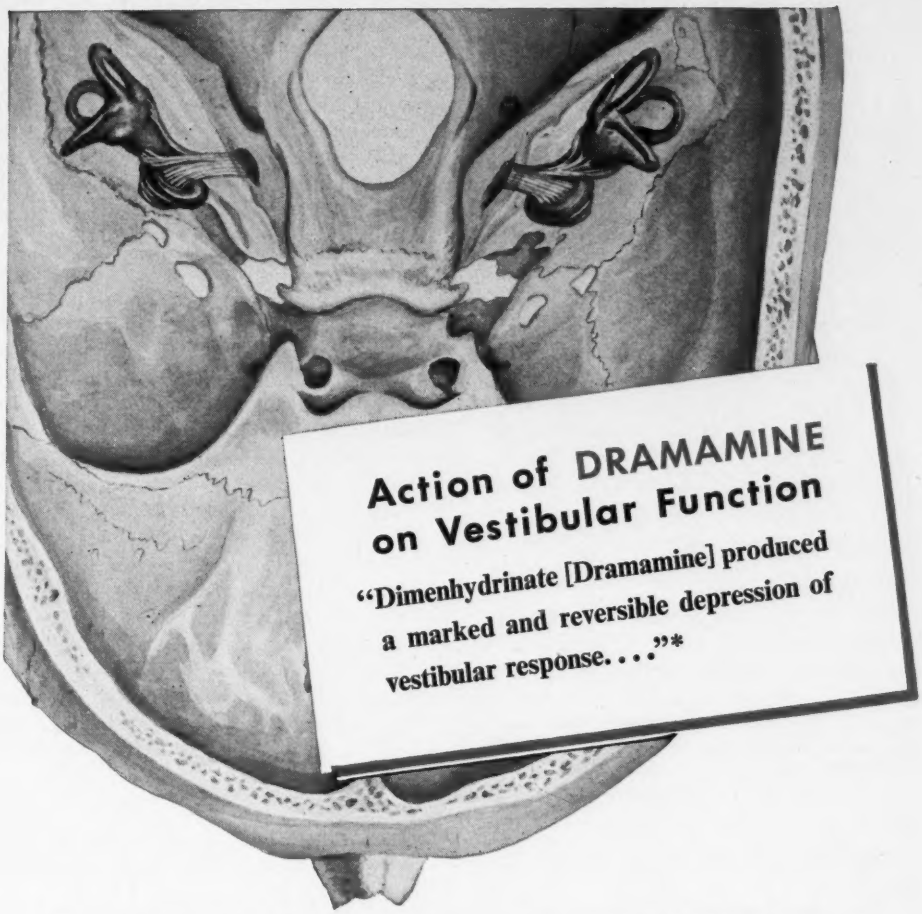
The average response of a single subcutaneous dose of protamine zinc insulin is demonstrable in four hours, reaches a prolonged peak in 24 hours, and is exhausted at the end of about three days. The peak effect of a single dose of protamine zinc insulin is weaker to the extent of one-fifth than that of a comparable dose of unmodified insulin, and correspondingly five times longer in duration.

With protamine zinc insulin it is possible to maintain prolonged insulin effect with infrequent injections. Control in mild diabetes is satisfactory with single daily doses, and even in severe diabetes there is smoother regulation of the blood sugar level. However, in severe diabetes its faults also become apparent. There is a definite tendency for the patient to develop postprandial glycosuria in the daytime and hypoglycemic shock at night.

To diminish this daily fluctuation, it has been the practice of many clinicians to so reduce the dosage

*This is one of 11 senior theses selected for publication by the Editorial Board from a group of 15 judged the best by the faculty of the University of Kansas School of Medicine.

**Thesis written while the author was a senior student at the University of Kansas School of Medicine. Dr. Hiesterman is now serving his internship at General Hospital, Kansas City, Missouri.


Action of DRAMAMINE
on Vestibular Function
"Dimenhydrinate [Dramamine] produced a marked and reversible depression of vestibular response. . . ."*

In a study of the action of Dramamine on vestibular function, Gutner and his associates found that Dramamine "significantly delayed the onset of nystagmus, shortened the duration of nystagmus and increased the milliamperage necessary to effect tilting."

The great effectiveness of Dramamine in motion sickness, they state, ". . . is probably related primarily to its ability to depress vestibular function. . . ."

DRAMAMINE®

BRAND OF DIMENHYDRINATE

—for prevention and treatment of motion sickness—

Now available in these dosage forms: { Tablets – 50 mg. / Liquid – 12 mg. per 4 cc. / Average dose – 50 mg.

ACCEPTED COUNCIL ON PHARMACY AND CHEMISTRY AMERICAN MEDICAL ASSOCIATION

*Gutner, L. B.; Gould, W. J., and Batterman, R. D.: Action of Dimenhydrinate (Dramamine) and Other Drugs on Vestibular Function, Arch. Otolaryng. *53*:308 (March) 1951.

RESEARCH IN THE SERVICE OF MEDICINE **SEARLE**

of protamine zinc insulin that nocturnal hypoglycemia does not occur and to control the daytime hyperglycemia with ordinary insulin given by separate injection. This produces better control than can be achieved with either protamine zinc insulin or unmodified insulin used alone. The addition of a small amount of unmodified insulin to the larger dose of protamine zinc insulin in the same syringe is ineffective, since it is precipitated by the excess of protamine and loses its prompt action entirely on mixing.

Globin Insulin with Zinc: This form of depot insulin is prepared by the addition of zinc and globin from beef hemoglobin in quantities sufficient to result in a type of action intermediate between ordinary insulin and protamine zinc insulin.

As marketed today it has the advantage over protamine zinc insulin in being a clear solution and requires no agitation to insure even distribution of the insulin when a dose is withdrawn from the ampoule. It is also claimed that globin insulin causes fewer allergic reactions than protamine zinc insulin.

The effect of a large dose of globin insulin in diabetes of moderate severity is recognizable in two hours, reaches a peak in eight to 12 hours, thereafter wanes and lasts about 24 hours. At its height its action is more intense than protamine zinc insulin but less than ordinary insulin.

Globin insulin, like protamine zinc insulin, controls mild diabetes easily, but its faults stand out prominently in severe diabetes. In single large doses it exhibits a decided tendency to cause late afternoon insulin shock and at the same time it often wanes so rapidly in effect that an overnight hyperglycemia develops, giving heavy glycosuria in the early morning hours. It fails to span the 24-hour period adequately and does not give the overlapping so essential for good control.

Protamine Insulin Mixtures and Modifications Because globin insulin and protamine zinc insulin fail to produce good control of severe diabetes by single daily injections, there has been a great deal of study on protamine zinc insulin modifications and with mixtures containing protamine zinc insulin and regular insulin.

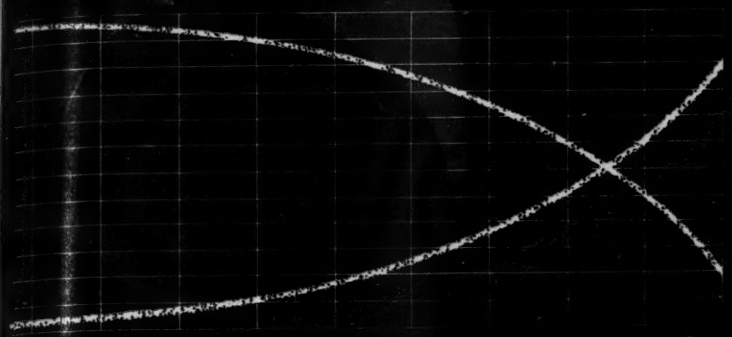
Colwell has demonstrated that excesses of regular insulin are necessary to produce appreciable alterations in the effect of protamine zinc insulin. His studies indicate that a mixture containing about twice as much regular insulin as protamine zinc insulin possesses the most desirable time activity to control severe diabetes by single daily injection. In a 2:1 mixture all the insulin is present in precipitated form and it is not a simple mixture of the two insulins of which it is composed. It represents an insulin-saturated protamine zinc complex which on injection releases its insulin more rapidly during

TABLE 1

Time-Activity of Single Large Doses of Various Types of Insulin in Diabetes of Moderate Severity (Approximate):*

Type of Insulin	*Action Demonstrable*	*Peak Action*	*Intensity at Peak*	*Duration of Effect*
Regular or Crystalline	1 hour	3-6 hrs.	Strong	8-12 hrs.
Globin with Zinc	2 hours	8-12 hrs.	Fairly Strong	24 hours at most
NPH Insulin	2 hours	10-20 hrs.	Moderate	28-30 hrs.
2:1 Mixture	4 hours	12-16 hrs.	Moderate	1½-2 days
Protamine Zinc	4-8 hours	24-32 hrs.	Weak	3 days or more

*From timing studies of Colwell with NPH insulin added.[4]



demand

supply

Stress states may bring about an increased *demand* for corticoid hormones that even a physiologically hyperactive adrenal cortex may fail to meet. In the shock following severe infections, burns, or major surgery, and in prolonged convalescence, the problem of *supply* may be answered by subcutaneous, intramuscular or intravenous injection of Upjohn Adrenal Cortex Extract.

Upjohn Adrenal Cortex Extract

Upjohn research in adrenal structure and function has aided the practice of medicine by the development of extracts which provide all of the natural adrenal cortical hormones.

Each cc. of Upjohn Adrenal Cortex Extract contains the biological activity equivalent to 0.1 mg. of 17-hydroxycorticosterone, as standardized by the Rat Liver Glycogen Deposition test. Heated 10′.

Supplied in 10 cc. and 30 cc. vials.

a product of

Upjohn

Research *for Medicine . . . Produced with care . . . Designed for health*

the first 12 hours than the second 12 hours. It is therefore more likely to control post-prandial glycosuria and less likely to cause nocturnal insulin shock.

In 1943, MacBryde and Roberts devised a somewhat similar modification of protamine zinc insulin in which protamine zinc insulin is suspended in a solution of insulin. It contains about 40 per cent as much protamine as protamine zinc insulin and is buffered so that about one-fourth of its insulin is in solution and three-fourths in the sediment. They designated this modification "NP 50."

Careful clinical and laboratory comparisons of the 2:1 mixture and NP 50 show them to be virtually indistinguishable in their time-activity. Both show reduction of sugar levels within four hours, attain their peak effect in 12 to 16 hours after injection, wane appreciably in effect at 24 hours, but maintain sufficient activity in the second day after injection to give desirable overlapping from dose to dose. In these respects they are actually intermediate in effect between protamine zinc insulin and globin insulin. Neither preparation is stable enough to meet rigid marketing specifications. There are also certain difficulties in the large scale production of a 2:1 mixture and NP 50 which are still not solved.

In patients requiring more than 20 units of insulin daily it has become popular in the past few years to use insulin mixtures freshly mixed in the syringe. Mixtures of 2:1 or 3:1 (regular insulin to protamine zinc insulin) are the ones most commonly used. This method requires the expenditure of considerable time by the doctor and patient. Actual demonstration of the technique is necessary and careful explanation and directions are imperative.

Additional objections to the procedure include: (1) increased chance for error in dosage, (2) dislike of some patients for the additional daily inconvenience, and (3) unsuitability for patients with limited intelligence or poor vision. Nevertheless, the reasonably satisfactory control of diabetes that usually results from properly adjusted tailor-made mixtures has justified their extensive use.

Modified Protamine Insulin (NPH-50; NPH Insulin): NPH insulin is a distinct entity. Its name is a composite of the following factors: N because it is neutral in reaction; P for protamine; H for Hagedorn who developed it; 50 because it is modified by the addition of 0.50 mg. of crystallized protamine for every 100 units of insulin—therefore, NPH-50 insulin, or, as it is more commonly called, NPH insulin.

The blood sugar lowering action of NPH insulin is relatively quick because it begins some two hours after injection, reaches its broad peak in 10 to 20 hours, and the duration of action is long, namely, 28 to 30 hours. From this description it is evident that NPH insulin somewhat resembles the 2:1 mixture of crystalline and protamine zinc insulin.

The duration of action is sufficient in most cases to assure an overlapping effect sufficient for satisfactory maintenance of blood sugar levels during fasting. Furthermore, the rather prompt onset of action of NPH insulin, being additive to the overlapping effect of the prior dose, is usually adequate to control the after-breakfast rise in blood sugar that formerly called for supplemental doses of unmodified insulin. In some severe cases, the action of NPH insulin may not be sufficiently intense in onset to prevent hyperglycemia after breakfast. In such instances it is advisable to add ordinary insulin to the NPH insulin as when mixtures have been used. The preparation does not absorb insulin to the same extent as does protamine zinc insulin. Therefore, one can anticipate a more direct reflection of the more rapid insulin effect.

Three hundred thirty-six patients of the Joslin Clinic were treated with NPH insulin. This group consisted largely of patients whose diabetes was characterized by its severity and in whom chemical control had been difficult. Of this group, 95 per cent were treated as successfully with daily injections of NPH insulin as with separate injections of crystalline and protamine zinc insulin. In only five per cent was NPH insulin less successful. The majority of these failures were in those patients whose requirements for long-acting insulin are small compared with their requirements for quick acting insulin.

Regulation of diet and exercise is a necessary adjunct to the treatment of diabetes with NPH insulin, just as it is with other forms of insulin now available. When administered before breakfast, the hypoglycemic hazard of NPH insulin is nocturnal rather than diurnal, although patients should be advised to watch for symptoms of hypoglycemia, particularly in the afternoon.

Wonderful though insulin is, the forms now available have three obvious defects: first, their administration is parenteral; second, their time of action is too slow, too short, or too long; and third, their hypoglycemic effect may be of abnormal degrees. The ideal insulin has been defined by Best and by Hagedorn as depot in type, one which would release insulin to the body when needed, and remain in depot when the blood sugar was within normal limits. Since this ideal insulin is not available, clinicians clamor for an insulin practical in nature with instant availability and with 24-hour action or more. NPH insulin has some of these desired clinical properties. It is considered by Kirkpatrick of the Mayo Clinic to be more convenient, safer and simpler than

Table without salt, mouth without saliva—

Randle Cotgrave (1611)[1]

The thought of meals without salt is unappealing to most patients who are placed on a salt-restricted diet.

The prescription of Neocurtasal can prove to be a most encouraging measure.

Neocurtasal is a "trustworthy, nonsodium-containing salt substitute"[2] designed to make the low sodium diet palatable.

For all salt (sodium)-free diets—Neocurtasal may be used wherever sodium restriction is indicated: congestive heart failure, hypertension, arteriosclerosis, pregnancy (to forestall tendency to fluid retention). It contains potassium chloride, ammonium chloride, potassium formate, calcium formate, magnesium citrate and starch. Potassium content 36%; chloride 39.3%; calcium 0.3%; magnesium 0.2%.

Neocurtasal®

SALT WITHOUT SODIUM

Available in 2 oz. shakers and 8 oz. bottles.

Winthrop-Stearns INC.
NEW YORK 18, N. Y. WINDSOR, ONT.

1. From Burton Stevenson's "Home Book of Proverbs, Maxims and Familiar Phrases:" Macmillan Co., 1948, p. 2028.
2. Heller, E. M.: The Treatment of Essential Hypertension. *Canad. Med. Assn. Jour.*, 61:293-299, Sept., 1949.

Neocurtasal, trademark reg. U. S. & Canada

either protamine zinc insulin or insulin mixtures.

Literally dozens of other insulin combinations with prolonged action have been described in the literature. To undertake a critical appraisal of their merits would be impossible for lack of comparative data. A summary of the type of combinations, their names, the dates of report, the investigators and the distinguishing characteristics has been prepared by Colwell, Izzo and Stryker.

Insulin Substitutes

The use of insulin for treatment of diabetes mellitus is an entirely satisfactory and successful therapeutic measure. The fact that insulin is ineffective when administered orally has led to efforts to obtain non-toxic insulin substitutes which are active when given by mouth. At present, however, no substance fulfilling these requirements has been prepared.

Many guanidine derivatives have a blood sugar reducing power. Several of these derivatives, of which Synthalin and Neosynthalin are the foremost examples, were used for a time in the treatment of certain diabetic cases. At first excellent results were claimed for both of them. Later work revealed that these compounds, after prolonged use, produced serious liver and kidney damage. Their clinical use has been practically discontinued.

A solution of colloidal sulfur on oral or parenteral administration, or rubbing sulfur into the skin will produce hypoglycemia in normal rabbits. Before the discovery of insulin, sulfur baths had frequently been employed in the treatment of diabetes, and favorable results were occasionally observed in mild cases.

Since finding that insulin is protein in nature many investigators have studied the possible hypoglycemic effect of the different amino acids, especially those which are present in the insulin molecule. Cystine, taurine, and cystamine show some hypoglycemic effect.

Collip and other workers have prepared extracts from various natural sources of which the following showed some antiglycemic activity: onion tips, sprouted grain, beet tops, beans, celery, cabbage, lettuce, mulberry leaves, wild carrot, sumac, American blueberries, Jerusalem artichoke, clam tissue, yeast, bacteria, and egg yolk. While extracts of these substances apparently reduce the blood sugar level, this phenomenon occurs only after a latent period of several hours to several days and the results are unreliable and unpredictable.

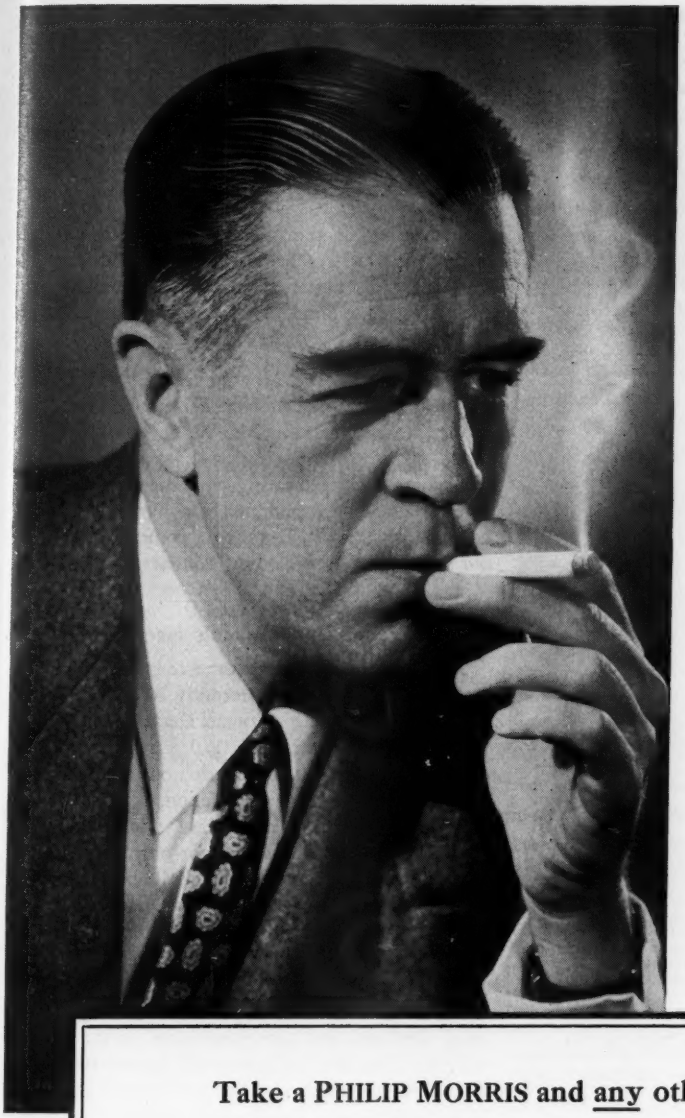
Clinical trials of insulin substitutes given orally have demonstrated on occasion a decrease in glycosuria during the course of treatment. However, the degree of glycosuria observed in cases of mild diabetes is a rather unsatisfactory index to the therapeutic efficiency of diabetic remedies, since the carbohydrate metabolism in such cases varies with both the diet and the general condition of the patient. Furthermore, it should be pointed out that the hypoglycemic action of insulin is not the only specific property of the hormone. An appreciable number of substances exist which will depress the blood sugar level in animals, but more careful work has generally shown that, in spite of the superficial similarity in effect, the physiological action of these substances is quite different from that exhibited by insulin itself. It is therefore obvious that every new insulin substitute should first be carefully studied in normal and depancreatized animals before its clinical trial on diabetic patients is attempted.

Summary

Outstanding features of insulin's chemistry and physiological actions are briefly outlined. Unmodified insulin, as far as is known, represents the true hormone in slightly acid solution. All modifications stem from it and do not alter its action except as they prolong the rate of activity. Protamine zinc insulin is the oldest of the modified insulins and has a weak but prolonged effect lasting up to 72 hours. Globin insulin, NPH insulin, and the 2:1 mixture all possess time-activity intermediate between insulin and protamine zinc insulin. At present it appears that most cases of diabetes mellitus can be well controlled by single daily injections of NPH insulin, thus obviating the use of mixtures and multiple daily injections except under special circumstances. Many other substances besides insulin have been shown to possess anti-glycemic activity, but to date no satisfactory insulin substitute has been found.

Bibliography

1. Adlersberg and Dolger: Insulin Mixtures in the Treatment of Diabetes, J.A.M.A., 128:414, 1945.
2. Beaser, S. B.: Diabetes Mellitus, N.E. J. Med., 243:3, July 20, 1950.
3. Beaser, S. B.: Diabetes Mellitus, N.E. J. Med., 243:4, July 27, 1950.
4. Colwell, A. R.: Effective Insulin Timing in Diabetes Mellitus, M. Clin. North Am., 327, March, 1947.
5. Colwell, A. R., Izzo, J. L., and Stryker, W. A.: Intermediate Action of Mixtures of Soluble Insulin and PZI, Arch. Int. Med., 69:931, 1942.
6. Colwell, A. R., and Izzo, J. L.: PZI Modified for Accelerated Action, J.A.M.A., 122-1231, 1943.
7. Colwell, A. R.: Nature and Time Action of Modifications of PZI, Arch. Int. Med., 74:331, 1944.
8. Colwell, A. R.: Protamine Insulin Mixtures in the Treatment of Diabetes Mellitus, New York State J. Med., 47:1103, 1947.
9. Duncan, G. G., and Barnes, C. E.: The Action of Globin Insulin Compared with that of Crystalline, Unmodified, and PZI, Am. J. M. Sc., 202:553, 1941.
10. Editorial: NPH Insulin, Physicians Bulletin, Sept.-Oct., 1950.
11. Editorial: The Chemistry of Insulin, Brit. M. J., 2:225, 1949.
12. Fortier, G.: The Antidiabetic Properties of Rhus Typhina (Sumac), Laval Med., 14:477 (Diabetes Abstracts. 9:3, 1950).
13. Gabriele, A. J., and Marble, A.: Clinical Experience with a New Modified Protamine Insulin (NPH-50), Am. J. Digest Dis., 16:197, 1949.
14. Guerra: Pharmacology of Antidiabetic Mexican Plants, Tecoma Mollis, and Contarea Latiflora, Diabetes Abstracts, 1948.



Doctor, be your own judge... try this simple test

With so many claims made in cigarette advertising, you, Doctor, no doubt prefer to judge for yourself. So won't you make this simple test?

Take a PHILIP MORRIS and <u>any</u> other cigarette

1. Light up either one first. Take a puff—get a good mouthful of smoke—and s-l-o-w-l-y let the smoke come *directly* through your nose.
2. Now, do exactly the same thing with the other cigarette.

You will notice a distinct difference between PHILIP MORRIS and <u>any</u> other leading brand.

PHILIP MORRIS

Philip Morris & Co. Ltd., Inc., 100 Park Avenue, New York 17, N. Y.

15. Hagedorn, H. C., Jensen, B. N., Krarup, N. B., and Wodstrup, I: Protamine Insulinate, Acta. Med. Scandinav. (Supp.) 78:678, 1936.
16. Handelsman, M. B.: Insulin in Diabetes, Bull. U. S. Army Med. Dept., 8:463, 1948.
17. Hildebrand, A., and Rynearson, E. H.: Clinical Experience with PZ and Unmodified Insulins, Arch. Int. Med., 72:37, 1943.
18. Houssay: Action of Sulfur Compounds on Carbohydrate Metabolism and on Diabetes, Am. J. M. Sc., 219:353, 1950.
19. Ibem: Modified PZI, Improvement on Standard PZI, J.A.M.A., 122:1225, 1943.
20. Jensen, H. F.: Insulin, Its Chemistry and Physiology, New York, Oxford Univ. Press, 1939.
21. Kirkpatrick, N. R.: Experiences with New Insulin, Proc. Staff Meet. Mayo Clinic, 24:365, 1949.
22. Krayenbuhl, C., and Rosenberg, T.: Crystalline Protamine Insulin, Rep. Steno Mem. Hosp., 1:60, 1946.
23. Lewis, J. J.: Cabbage Extracts and Insulin-like Activity, Brit. J. Pharm., 5:21, March, 1950 (Diabetes Abstracts, 9:4, 1950).
24. MacBryde, C. M., and Roberts, H. K.: Modified PZI, an Improvement on Market PZI, Proc. Central Soc. Clin. Research, 15:7, 1942.
25. MacBryde, C. M., and Roberts, H. K.: A New Modified PZI, Comparison with Histone Zinc Insulin, Clear and Standard PZI, J. Clin. Inves., 22:791, 1943.
26. Palmer, L. J., and Peck, F. B.: Official Syringe of the Am. Diabetes Assn., J.A.M.A., 139:7, 1949.
27. Peck, F. B.: The Insulins in Diabetes, Mod. Med., 17:64, 1949.
28. Peck, F. B.: Insulin Mixtures and Modifications, M. Clin. North Am., 343, March, 1947.
29. Pollack, H.: The Handling of Insulin, A D A Forecast, 3:1, Jan., 1950.
30. Reiner, L., Searle, D. S., and Lang, E. H.: On Hypoglycemic Activity of Globin Insulin, J. Pharm. and Exp. Therap., 67:330-340, 1939.
31. Rohr, J. H., and Colwell, C. R.: Comparative Time Action of Globin Insulins, Arch. Int. Med., 82:54-62, 1948.
32. Sanger, Species Differences in Insulins, Nature, London, 164:529 (Diabetes Abstracts, Vol. 9 No. 4, 1950).
33. Sclessor, A., and Nicol, T.: Di-insulin, a Clinical Trial, Lancet, 1:820, 1947.
34. Scott, D. A., and Fisher, A. M.: Studies on Insulin with Protamine, J. Pharm. and Exp. Therap., 58:78, 1936.
35. Scott, C. A., and Fisher, A. M.: The Effect of Various Substances on the Action of Insulin, J. Pharm. and Exp. Therap., 58:93, 1936.
36. Sharkey, T. P.: New Modified PZI (NPH-50) Ohio State M.J., 46:446, May, 1950.
37. Sparks, M. I., and John, H. J.: The Clinical Use of Mixtures of Insulin, Ohio State M.J., 39:226, 1943.
38. Sprague: Mixtures of PZI and Regular Insulin, Ann. Int. Med., 31:628, 1949.
39. Stetten, D., Jr.: Carbohydrate Metabolism, Am. J. Med., 7:571-584, 1949.
40. Ulrich, Helmuth: Clinical Experiments with Standard and PZI, Ann. Int. Med., 14:1166, 1941.
41. Weisel: Insulin Mixtures, Am. J. Med., 7:655, 1949.
42. White, P.: Modified Protamine Insuline (NPH-50), A Clinical Report, J.A.M.A., 141:312, 1949.
43. Wilder, R. M.: Insulin Mixtures and Conservation of Insulin, Am. J. Med., 5:532, 1948.
44. Kuppers-Sonnenberg, G. A. (Europe): Prophylactic Control of Diabetes Mellitus with Jerusalem Artichoke, Therap. d. Gegnw., 6:176-78, Jan., 1949 (Diabetes Abstracts, 1950).

COUNTY SOCIETIES

A meeting of the Shawnee County Society was held at the Hotel Jayhawk, Topeka, on February 5. Dr. Galen M. Tice, of the University of Kansas Medical Center, Kansas City, spoke on "Pediatric Roentgenology." With this meeting the society returned to a former practice of having a dinner precede the scientific and business sessions.

* * *

Officers of the Smith County Society were elected at a meeting held January 22 at the home of Dr. Victor E. Watts, Smith Center. Dr. F. H. Relihan was named president; Dr. Lafe W. Bauer, vice president; Dr. Watts, secretary; Dr. Buford Hartman and Dr. Bauer, delegates to the state meeting to be held in April.

The Nemaha County Society met in Sabetha on January 22. Dr. J. Stone, a dentist, who recently returned from Korea, told of his experiences. The following officers were elected: president, Dr. C. C. Hunnicutt, Sabetha; vice president, Dr. J. H. Gilbert, Seneca; secretary, Dr. T. A. Montgomery, Sabetha.

* * *

A meeting of the Wilson County Society was held at the Blue Tea Room, Neodesha, February 13. Mrs. Margaret Foster, Topeka, a representative of Blue Cross-Blue Shield, was speaker of the evening.

* * *

A meeting of the Montgomery County Society was held in Independence on February 20 with the county welfare director, Mr. W. O. Campbell, as a guest. Medical service for welfare recipients was the subject of the meeting, and the president, Dr. J. D. McMillion, appointed Dr. Porter M. Clark and Dr. William R. Beine to a committee to work out details of a possible new contract.

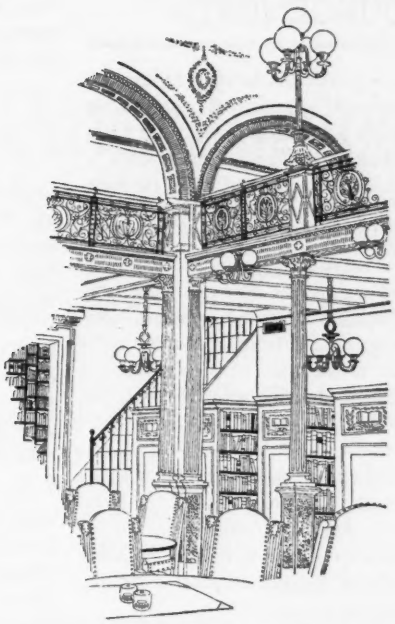
Experimental Animals Necessary

The necessity for using experimental animals in research was pointed out recently by Dr. C. J. Van Slyke, director of the National Heart Institute, who stated that approximately 170 cardiovascular research projects now being carried out are dependent upon such animals for completion.

"The problem of heart disease is increasingly serious," Dr. Van Slyke said, "not only because it is the leading cause of death and disability, but because of a growing and aging population. Investigators carrying forward heart research under National Institute grants have found that the laboratory animal plays a vital role. Animal studies must precede application of new methods to human beings. The need has been established on the basis of the fact that most of the great discoveries to improve human health in the past 50 years have been at least in part the direct result of animal studies."

Mentioned as an example was a technique developed toward the eventual repair of defects of the muscular wall inside the human heart. Such defects have been closed in the hearts of dogs with two part-plastic buttons.

Seven scientists receiving heart research grants have recently reported progress on the perfection of an artificial heart, or combination heart-lung machine. They have been able to carry the circulation of dogs in their machines for as long as 127 minutes. Motion pictures have been made which illustrate the operations and the healthy condition of the animals following the mechanical heart-lung substitution.



from

among all

antibiotics

Pediatricians

often choose

AUREOMYCIN

Hydrochloride Crystalline

because... Aureomycin may be given by the oral, or in an emergency by the intravenous, route. Aureomycin readily and rapidly diffuses into all the tissues and fluids of the body.

Aureomycin in divided small dosage has given serum levels comparable with those following one large dose.

Aureomycin is clinically effective in the control of infections of bacterial, rickettsial, and large viral origin.

Aureomycin has been reported to be effective against susceptible organisms in: Bronchiolitis • Bronchitis • Colitis • Epidemic Diarrhea • Childhood Genitourinary Infections • Laryngotracheobronchitis • Secondary Infections following Measles • Mucoviscidosis (pancreatic fibrosis) • Neonatal Infection • Otitis Media • Mastoiditis • Pertussis Pneumonia • Scarlet Fever • Secondary Invasion following Varicella

Throughout the world, as in the United States, aureomycin is recognized as a broad spectrum antibiotic of established effectiveness.

Capsules: 50 mg.—Bottles of 25 and 100. 250 mg.—Bottles of 16 and 100.
Ophthalmic: Vials of 25 mg. with dropper; solution prepared by adding 5 cc. of distilled water.

LEDERLE LABORATORIES DIVISION AMERICAN CYANAMID COMPANY 30 Rockefeller Plaza, New York 20, N.Y.

ANNOUNCEMENTS

A contest open to physicians serving residencies or internships in medicine in approved hospitals has been announced by the Kansas City Southwest Clinical Society, 630 Shukert Building, Kansas City 6, Missouri. Applications for participation in the contest must be made in writing to the executive office of the society on or before May 15, 1952.

Papers submitted must be original work of the physician, compiled during his service in the hospital, including experimental laboratory work. Contestants must have graduated from approved medical schools and must be members of their respective county or state medical societies, effective with the graduating class of 1945 to date.

* * *

The American College of Allergists will hold its annual meeting at the William Penn Hotel, Pittsburgh, Pennsylvania, April 7-9. Physicians are invited to attend and may secure additional information from the College, LaSalle Medical Building, Minneapolis 2, Minnesota.

In addition to 20 addresses on general topics and scientific investigations, there will be round table luncheons and sectional meetings devoted exclusively to the psychosomatic aspects of the allergic patient, allergy in infants and children, allergic manifestations in the skin, eye, ear, nose and throat. One session will be devoted to the problems of the allergic patient as met in industrial medicine.

Preceding the meeting, on April 4-6, the College will offer a graduate instructional course in allergy with 60 well known authorities taking part in the program, designed especially for general practitioners.

* * *

The Fifth American Congress on Obstetrics and Gynecology will be held in Cincinnati's Netherland-Plaza Hotel, March 31 through April 4, under the sponsorship of the American Committee on Maternal Welfare. Included on the program will be a report on proposed legislation for Emergency Maternal and Infant Care by Dr. Joseph Lawrence, director of the A.M.A. Washington office. Techniques, conclusions and follow-up action in Chicago's recent study of 10,000 neonatal deaths will be presented in a symposium.

* * *

The annual dinner meeting of the Wichita Foundation of Medical Research will be held on Monday, May 26, at 6:30 p.m. at the Hotel Lassen, Wichita. Dr. T. G. Blocker, Jr., professor of plastic surgery at the University of Texas School of Medicine, Galveston, will speak on "Research Problems in Plastic Surgery." All physicians are cordially invited to attend and may secure information and reservations from Dr. M. M. Tinterow, 306 KFH Building, Wichita 2, Kansas.

Speedy X-rays for Army

To increase further the mobility of its forward surgical hospitals in Korea and to accelerate screening of casualties, the Army Medical Service recently announced that it would begin using a new, portable field x-ray unit and 60-second developer as soon as shipment can be made to the combat theater.

The 500-pound machine, half the weight of the model now in use, can be completely assembled or dismantled in five minutes. It can be transported by jeep, airdropped, or subjected to the most unfavorable atmospheric conditions without impairing its efficiency.

It consists of two metal chests, including a portable field generator. The high-speed developer produces finished, positive x-ray film in 60 seconds. During complex fracture surgery when x-rays are taken throughout the operation to determine the exact position of bones after each manipulation, fast developing will be particularly valuable. The developing unit requires neither liquid chemicals nor darkroom processing, and instead uses a gelatin-like capsule of chemicals to produce a clear image which may be read without the aid of an illuminator.

The 93rd annual meeting of the Kansas Medical Society will be held in Kansas City, Kansas, April 27 through May 1, with scientific sessions beginning on Tuesday, April 29. Hotel reservations are to be made through the Kansas City Chamber of Commerce, Town House, Kansas City, Kansas.

DEATH NOTICES

JAMES WALDO RISDON, M.D.

Dr. J. W. Risdon, 74, an active member of the Leavenworth County Medical Society and a past president of that group, suffered a fatal heart attack while playing golf at the Leavenworth Country Club on January 30. He was graduated from the University Medical College, Kansas City, in 1905, and immediately after began practice in Leavenworth. For the past 33 years he had been practicing in association with Dr. D. R. Sterett, specializing in surgery. He was active in Rotary Club work and had served as president of the Leavenworth club.

Your Laboratories . . .
Our Responsibility

Duncan Laboratories
Established 1921

KANSAS CITY, MO.,
909 Argyle Bldg.
JOPLIN, MO., *230 Frisco Bldg.*

Associated Laboratories

INDEPENDENCE, MO.
Physicians Laboratory
First National Bank Bldg.

LEXINGTON, MO.
Lexington Memorial Hospital

SEDALIA, MO.
Bothwell Memorial Hospital

WARRENSBURG, MO.
Warrensburg Medical Center

Curbstone Consultation

All diabetic patients should have a chest X-ray once a year because

THE INCIDENCE OF TUBERCULOSIS AMONG DIABETIC PATIENTS AS COMPARED WITH NON-DIABETIC PATIENTS IS THREE TIMES GREATER IN ADULTS, 13 TIMES GREATER IN CHILDREN OF SCHOOL AGE, 16 TIMES GREATER AMONG ADOLESCENTS.

Theoretically, this increased susceptibility is due to the imperfect epithelialization of the respiratory tract due to the inability of the diseased liver of the diabetic to convert carotene into vitamin A.

Banyai and Cadden, Arch. Int. Med., p. 445-6, 1944.
Foley and Andosca, Med. Cl. North Amer. 28, p, 499-505, March, 1944.

Pathologically Speaking

THE FROG TEST FOR PREGNANCY

WITHIN the past five years, the advantages as to accuracy, speed of performance, and simplicity of technique of the frog test for pregnancy have been recognized in most clinical laboratories.

Accurate diagnosis in the first half of pregnancy occurs in about 95% of cases, but the incidence of false negatives in the latter half of pregnancy increases. To date, only rare false positives have been reported, one presumably related to estrogen therapy in the patient and a few others occuring in patients with jaundice; most investigators report no false positives in large series of cases.

Either the first morning specimen of urine or blood serum obtained in the fasting state is used. It is always preferable to obtain blood from the patient since one may at any time encounter the woman who submits a urine specimen from another individual for purposes of obtaining an opposite report.

Serum and/or urine is injected into the dorsal lymph sac of the ordinary male frog. The subsequent release of sperm by the frog constitutes a positive test for pregnancy. In most cases, the frog will have passed sperm (or they can be obtained via capillary tubing from the cloaca) within two hours following injection; many positive tests show sperm within 30 minutes after injection.

Occasionally a specimen which yields a false negative result in the frog may register positive in the rabbit, and hence it is the practise in many laboratories (including ours) to follow all negative frog tests with a Friedman.

RALPH EMERSON DUNCAN, M. D.
LORAINE E. SCHULTZ, M. D.
ALBERT E. UPSHER, M. D.

THE KANSAS PRESS LOOKS AT MEDICINE

Editor's Note. In this section the Journal reproduces editorials relating to medicine which have appeared in the lay press. An effort is made to include both favorable and unfavorable comments, and the Editorial Board in no instance assumes responsibility for the opinions expressed.

Taxes Well Spent

One cannot visit the KU Medical Center in Kansas City, Kansas, even briefly, without coming away full of admiration and praise for the progress all Kansas medicine is making there.

It's a never-ending job, teaching hundreds of young men and women to be the doctors and nurses of an early tomorrow. To do it this huge medicine center has collected an excellent practicing faculty. It runs large clinics at which young physicians have the chance to observe experienced staff physicians at work in all the various specialties. The clinics of course are a godsend to the thousands of people in that area who could not otherwise afford good medical care.

On the KU medical center site, the sound of the builder is never stilled. More new buildings are being erected, still others are being planned. The medical center which will serve this state tomorrow is going to be a bigger and better one than the one we have today.

We have teams of medical experts today who go out regularly on clinic trips over the state, keeping the practicing Kansas physician abreast of the latest advances in medical science.

The next step possibly may be clinical centers of more permanent nature located in various parts of the state which will present the facilities for spreading even more the vast wealth of information and know-how techniques the KU center has collected.

Certainly the tax dollar which goes into the medical center and this mushrooming educational program is well spent. The program launched by Dr. Franklin Murphy, which has won national acclaim, is not to be sidetracked, neglected, or stalled.

As long as American medicine can sponsor within itself the great surge we have today in Kansas, the false theory of socialized medicine will make no great inroads here.—*Garden City Telegram, February 19, 1952.*

New Type of Resuscitator Developed

A mechanical artificial resuscitator, so light and compact that it can be carried in the standard gas mask carrier along with the mask, has been developed by the Army Chemical Corps and is now being standardized. It can be operated in combat by one man.

The device was developed specifically to provide treatment under combat conditions for troop casualties that might result from an enemy attack with gases.

The new resuscitator is a modification of the mouth-to-mouth forced breathing that is frequently used on choking babies. It consists of a length of corrugated rubber tubing that is connected to the gas masks of both the operator and the victim. The operator inhales clean air through his own canister and by exhaling forces it into the lungs of the victim. The victim exhales through a valve in the side of the tube. Tests show that the forced breathing is not unduly tiring to the operator and can be carried on for more than an hour.

Program for Aging Workers

Government and industry were urged to discard the economically-wasteful and socially harmful policy of compulsory employee retirement at age 65 at a conference on aging held in January under the auspices of the National Social Welfare Association and the McGregor Fund of Detroit. Attending were 75 experts in industrial relations, medicine, labor and education.

The conferees agreed that retirement solely on the basis of age was socially wasteful and that "older persons willing and able to meet job requirements could make a positive contribution to the national economy." The country is now losing the potential labor of 1,500,000 persons. Plans should be made for a constructive program to deal with the growing problem of older persons.

Dr. Theodore G. Klumpp, president of Winthrop-Stearns, Inc., declared that retirement by chronological age would become a "crisis" in 30 years unless "solutions are found to keep a growing older and healthier population out of idleness." He noted that by 1980 we will have some 66,000,000 persons over 45 and something in the neighborhood of 24,000,000 of age 65 and over.

Industry representatives at the conference were at odds over the retirement problem. One view held that the individual worker should be permitted to make the decision, while others felt that compulsory retirement at 65 had worked well and was economically desirable.

A number of experts cautioned that the cost of maintaining an aging population would become prohibitive and that such a population might develop a social-political force threatening the existing mores in the community.

"PREMARIN"®

Highly effective • Well tolerated • Imparts a feeling of well-being

"PREMARIN"

Most menopausal patients
experience striking relief
of symptoms with "Premarin."

"PREMARIN"

Estrogenic Substances (water-soluble)

"PREMARIN"

also known as Conjugated Estrogens (equine)

"PREMARIN"

8202 AYERST, McKENNA & HARRISON Limited • New York, N. Y. • Montreal, Canada

Ayerst

BOOK REVIEWS

Introduction to Medical Science. By Jensen and Noller. Published by C. V. Mosby Company, St. Louis. 533 pages, 71 illustrations. Price $5.75.

Since the growth of the Integrated Teaching Program, nursing schools no longer give and label a course as "Introduction to Medical Science." However, this book has many areas which would be valuable for reference to students throughout their entire training period.

The unit "Development of Medical Science" is concisely written in an interesting manner and should be helpful. The separate presentations of signs and symptoms should save the usual confusion in these areas. Many illustrations, including radiographic illustrations, help make the clearly written section of "How the Doctor Makes the Diagnosis" excellent. The nurse doesn't need complete information on test methods. In this section she can quickly find a wealth of help.

One wonders why nursing care was included. Only two brief pages are given to it. Most of this brief area is given to discussion of physical well being and mentions only the great support she can give and a definite need for her to understand the mental needs of her patient.

The nurse would find very little help in the unit of "How Disease is Treated."

It is a pleasure to find a large, valuable and interesting area on "Control and Prevention of Disease."

"Introduction to Medical Science" should be a favorite and well used reference authority for students in all areas of their training as well as for alert graduate nurses.—*H.A.*

* * *

Biological Antagonism: The Theory of Biological Relativity. By Gustav J. Martin. Published by the Blakiston Company, Philadelphia. 516 pages, 64 figures, 44 tables. Price $8.50.

This compact book summarizes a great deal of the knowledge that has been accumulated by one of our newest biological sciences. Written by a chemist, it deals at greatest length with chemical phenomena although it contains items of interest to the pharmacologist and chemotherapist.

The main thesis of the book is that in the field of biology, as in the physical sciences, or more so, all things are relative; there are no examples of absolute specificity. The thesis is further developed that biological reactions, chemotherapeutic efficacy and pharmacologic responses are dependent upon one of two general actions: the displacement of a metabolite or the inhibition of an enzyme system.

The importance of protein as building block, enzyme and "receptor" is pointed up; in the system of biological relativity protein is the key. Interestingly, it is shown that the shape of the protein, either fibrous or globular, determines to a large extent what function the protein will have. Finally, the essential similarity between enzymes and what we called, for want of a better term, "receptor" is clarified.

This book is pointed toward the biochemist and pharmacologist although it will make interesting reading for any student of the biological sciences. It should be added that it is weakest in its discussion of pharmacology and strongest in its discussion of biochemistry. Although the reading is sometimes tedious there is, at the end of each chapter, a brief recapitulation that serves to orient the reader to the thesis that is being developed.—*W.C.W.*

* * *

Untoward Reactions of Cortisone and ACTH. By Vincent J. Derbes and Thomas E. Weiss. Published by Charles C. Thomas, Springfield, Illinois. 77 pages. Price $2.25.

This very timely monograph on the untoward reactions from cortisone and ACTH should be in the library of every physician who uses these potent drugs.

An excellent bibliography is included at the end of the monograph.—*W.L.V.*

Help for Cerebral Palsied

Encouraging progress in improving the condition of the cerebral palsied during the past year was reported recently at a meeting of United Cerebral Palsy in Chicago. Donations in 1951 more than doubled the previous year's total, $1,022,000, showing that the American people are becoming more aware of the gravity of this need.

The additional funds have made possible the expansion of services, increase in existing facilities for diagnosis, treatment, care and education; establishment of new clinics and treatment centers, and the initiation of research and training projects totaling $169,679 in 18 universities and hospitals. Scientists and physicians interested in the problem of cerebral palsy may apply for grants to United Cerebral Palsy, 50 West 57th Street, New York 19, New York.

A new book, *Environment and Health,* was recently published by the U. S. Public Health Service to stress the fact that "the modern concept of health is not simply freedom from suffering but the positive enjoyment of life in wholesome surroundings." Copies may be secured from the Superintendent of Documents, Government Printing Office, Washington 25, D. C.

citrus is virtually

NON-ALLERGENIC

TYPICAL PATCH TEST

Over 400 infants and children from 2 weeks to 6 years of age acted as test subjects to check the incidence of sensitivity to orange juice. After 2 to 12 months' observation,* "no disturbance of bowel function (diarrhea or constipation) that could be attributed to the orange juice" was found. Also, the occurrence of regurgitation and rashes was "minimal". In the rare instances of sensitivity, care exercised by gentle reaming of juice (or the use of frozen concentrate) to avoid contamination with peel oil usually obviates the difficulty.

**J. Pediat. 39:325, 1951*

FLORIDA CITRUS COMMISSION • LAKELAND, FLORIDA

FLORIDA *Citrus*

ORANGES • GRAPEFRUIT • TANGERINES

ABSTRACTS FROM CURRENT LITERATURE

Arterial Hypertension

Arterial Hypertension: Prognosis. By Arthur H. Greip, Winston Hall, George R. Barry and Sibley W. Hooble, Am. Jnl. Med. Sci., 221:3, 239-249, Mar., 1941.

The authors studied 117 consecutive patients under age 53 with blood pressures which exceeded 160/110 on two or more occasions and who were observed over a period of eight to 10 years. When originally studied, these patients had neither primary renal disease, coronary thrombosis, recent cerebrovascular accidents, congestive failure or severe renal impairment. The report deals with three aspects: 1. Gross mortality rate and type of death; 2. Factors influencing prognosis; 3. Status of the survivors.

1. Of the 117 patients, 46 per cent died from hypertensive complications (equally divided between cardiac and cerebrovascular accidents), two per cent from unknown causes, six per cent from reasons unrelated to high blood pressure. Forty-six per cent were alive at the end of the 10-year interval. Uremic deaths were uncommon.

2. (a) Sex influenced prognosis in that females with comparable hypertension outlived males in a ratio of 3:2.

(b) Initially observed hypertensive complications (i.e.: electrocardiographic abnormality, cardiac enlargement, history of cerebrovascular accident or focal encephalopathy) indicated a poor prognosis.

(c) Initial high diastolic pressure tended to predispose to the hypertensive complications mentioned above, and this provided a poor prognosis. Excluding such complications, it was by no means certain that blood pressure levels bear any important relation to prognosis.

(d) The effect of the patient's age and the duration of hypertension was of prognostic significance as follows: Uncomplicated hypertension in older patients had a slightly higher mortality rate but complicated hypertension had a definitely higher mortality in the younger age groups. The known duration of hypertension had no prognostic importance.

(e) Cardiac complications proved bad prognostic evidence. Enlargement was more serious than EKG abnormalities. As many deaths in this group were cerebrovascular as cardiac.

(f) Viewed from the aspect of CNS symptoms, nothing was conclusive. Those patients with headaches and dizziness had no higher mortality rate than a similar number who had no such complaints. Retinopathy was more frequently a precursor of CVA than any subjective complaint.

(g) Retinopathy was not observed to foretell the type of death but was a guide to the degree of vascular degeneration.

(h) Concerning the renal status and prognosis, persistent albuminuria was the most dependable sign, though decreased urea clearance as an evidence of impaired renal function foretold a poor prognosis.

(i) Blood pressure changes deserve mention. There was a general tendency for it to fall slightly in cases with cerebral deaths and to rise in patients with cardiac deaths. There was no evidence that a rising blood pressure predisposed to cerebrovascular accidents.

3. Of the 51 living patients, 19 were asymptomatic, 61 per cent had mild symptoms and all, totaling 80 per cent of this group which is 35 per cent of the entire series, were capable of doing their daily work. Forty-three per cent of all the females and 13 per cent of all the males fell in this category. The gross mortality over a nine-year period was 50 per cent compared to an expected mortality of 7.8 per cent for the same interval of the normal U. S. population of the same age, sex and color distribution.

In order of individual importance, the following aspects influenced prognosis: Hypertensive complications: cardiac enlargement, persistent albuminuria, history of encephalopathy or cerebrovascular accident; 2. Height of the diastolic pressure; 3. Male sex; 4. Abnormality of the EKG; 5. Hypertensive retinopathy.

Factors that did not have prognostic significance: age of the patient, duration of the hypertension, frequency and severity of headaches and dizziness.—*P.W.M.*

* * *

Inferior Vena Cava Ligation

Late Sequelae of Inferior Vena Cava Ligation. By Patrick C. Shea and L. Robertson, Surg., Gyn. and Obs., 93, 153-158, Aug., 1951.

This study is based upon 37 patients in whom ligation of the inferior vena cava had been performed between 1943 and 1950. Twenty-five of these were suitable for evaluation, records being incomplete on the remainder. Only one patient is entirely free of adverse results. Sequelae usually follow one or two patterns: 1. A small group which develops arteriospastic changes leading in some instances to reflex dystrophies, dermatoses and ulcera-

It's Convenient to Buy Kanox

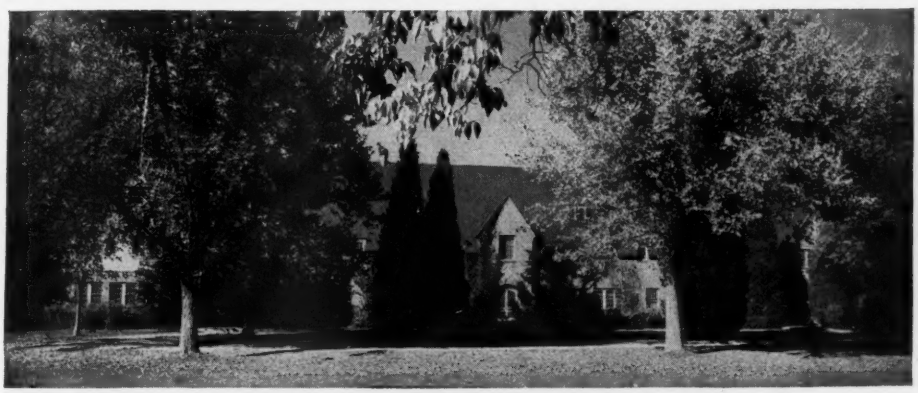
THERAPEUTIC OXYGEN AND ANESTHETIC GASES

Oxygen Therapy
Regulators and Equipment
Repair Service for
Regulators, Flowmeters
and Humidifiers

Nitrous Oxide
Ethylene
Carbon Dioxide
Helium
Oxygen
Cyclopropane

KANSAS OXYGEN, Inc.

Phone 6392 HUTCHINSON, KANSAS Box 551



Woodcroft Hospital--Pueblo, Colorado

A private hospital for the scientific treatment of neuro-psychiatric disorders, including alcoholism and drug addiction. Beautiful landscaping and home-like surroundings afford a restful atmosphere. Accommodations vary from single rooms with or without bath to rooms en suite, allowing for segregation of guests.

Detailed information furnished on request.

Karl J. Waggener, M.D.

tion; 2. The larger group develops edema which also may eventuate in ulceration.

The authors believe that the ligation, per se, is responsible for most of these changes and do not agree with the theory that sequelae are due to persistence or recurrence of the disease process in the vessels themselves. In some instances, patients with extensive vascular disease of the lower extremities had lesser sequelae.

It is concluded that vena cava ligation should be employed only for those persons who have experienced multiple infarctions after other methods of therapy have failed.—*T.P.B.*

* * *

Acute Nephritis in Schoolboys

Outbreak of Acute Nephritis in Adolescent Schoolboys. By C. Henry Kempe et al, Ped., 8:3, 393-405, Sept., 1951.

The occurrence of acute nephritis in groups of associated persons has been noted in a variety of different circumstances. Among soldiers it is called trench or war nephritis. It may occur in congested tenement districts and among families where several children develop nephritis simultaneously or in rapid succession. The authors report an outbreak of acute nephritis which occurred among adolescent boys who were students at a private day school.

Four boys in one class had clinically typical acute glomerular nephritis.

Seventeen other members of this and one other class were found to have hematuria with or without associated albuminuria. The total incidence of hematuria among the 73 students in these two classes was 29 per cent. Fifteen of the 21 boys with hematuria still had abnormally elevated Addis counts approximately seven weeks after the initial examination.

Cultures of the nasopharynx were made from 85 students. Hemolytic streptococci were detected in 11 (13 per cent) of the boys including three with hematuria. The results of attempts to identify the streptococci by serologic technics indicated that at least five immunologically different varieties were represented.

These cases suggest that it would probably be good medical practice to check urines on possible associated groups in order to pick up mild cases of nephritis which might be overlooked and continue in a chronic nephritis.—*D.R.D.*

Recommend Discarding Heroin

To protect public health and safety an international pharmacologists' group has recommended that diacetylmorphine (heroin) no longer be used for medical purposes, and should be replaced in all countries with other, less dangerous drugs.

The World Health Organization's expert group on narcotics which meets regularly to advise on problems connected with drug addiction, also examined the addictive properties of some 15 new synthetic substances, several of which are already on the market. The substances examined belong to the pethidine, methadone and morphinan types and are potent analgesics. Thirteen of these drugs should be under international control, the experts recommended.

The recommendation on heroin was taken after the group learned that, on the World Health Organization's request, 50 countries have already discontinued or are willing to discontinue the medical use of heroin.

Governmental authorities have been greatly concerned for several years by excessive increase in heroin consumption. Large quantities are finding their way into illegal channels. Until recently, however, there was widespread reluctance to suppress medical use of the drug because of its qualities as a pain killer and cough suppressive. Experience has shown that it can now be replaced by other morphine derivatives or by new synthetic substances.

The problem of chronic abuse of sleep-producing drugs was also studied. Several countries are producing these drugs in increasing quantities, often exceeding the amount needed for therapeutic purposes. It is difficult to differentiate between the various barbiturates with respect to the intensity of addiction liability, and the experts therefore believed that international control was premature.

Of all babies born in the United States in 1949, 86.7 per cent were born in hospitals. In 1935 the figure was only 36.5 per cent.

A difference of only 10 calories per kilogram of body weight can mean success or failure of the growth of healthy children eating a good mixed diet. This was revealed by a careful study of the food intake, metabolism, and growth of 10 healthy children, four to nine years of age, over a period of 69 months. The investigators found that nitrogen retention was depressed when the caloric intake was insufficient. The appetites of the children could not be relied upon to insure consumption of enough food to allow satisfactory weight gain. The study supports the validity of the daily calorie allowance for children as recommended by the Food and Nutrition Board of the National Research Council.—*Journal of Nutrition, 45:189, Oct., 1951.*

"The practice of medicine is so divided among them that each physician is a healer of one disease and no more."—Quotation attributed to Herodotus, the Greek historian, about 1500 B.C.

AMERICAN BOARD EXAMINATIONS

Anesthesiology. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15, Conn. Various locations, July 18.

Dermatology and Syphilology. Sec., Dr. George M. Lewis, 66 East 66th St., New York 21. Written, Chicago, March 1952. Oral, Chicago, May, 1952.

Internal Medicine. Sec., Dr. William A. Werrell, 1 West Main Street, Madison 3. Written, various centers and overseas, Oct. 20; closing date for applications, May 1. Oral, Cleveland, Apr. 17-19; Chicago, June 5-7; San Francisco, in fall.

Obstetrics and Gynecology. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6. Oral, Chicago, June 7-13, 1952.

Ophthalmology. Sec. Dr. Ewin B. Dunphy, 56 Ivie Road, Cape Cortage, Maine. Oral, Oct. 6-10, Chicago. Practical, Philadelphia, May 29-June 3; Chicago, Oct. 6-10; New York City, June 6-10.

Otolaryngology. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City. Oral, Chicago, Oct. 6-10.

Pathology. Sec., Dr. Robert A. Moore, 1402 S. Grand Blvd., St. Louis.

Pediatrics. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa. Oral, Washington, D. C., May 3-5; San Francisco, late June; Chicago and Boston, in fall.

Physical Medicine and Rehabilitation. Sec., Dr. Robert L. Bennett, 30 N. Michigan Ave., Chicago. Parts I and II, Chicago, June 8-9.

Preventive Medicine and Public Health. Sec. Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore. Written, Apr. 18, Berkeley, Calif., Minneapolis, New Orleans, Baltimore.

Psychiatry and Neurology. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn. New York City, Dec. 15-16; closing date for applications, Sept. 15.

Radiology. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

Surgery. Sec., Dr. J. Stewart Rodman, 225 South 15th St., Philadelphia. Written, various centers, March, 1952, Oct., 1952.

Urology. Sec., Dr. Harry Culver, 30 Westwood Road, Minneapolis 16. Chicago, Feb. 9-13, 1952.

Deformity Appliances of Quality

Orthopedic and Surgical Appliances
Artificial Limbs

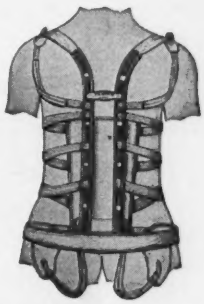
Trusses

Abdominal Supports

Elastic Hosiery

Foot Supports

Surgical Corsets



Taylor Back Brace

Made to Order In Our Own Factory

P. W. HANICKE MFG. CO.
1009 McGee St. Victor 4750
KANSAS CITY, MO.

THE MAJOR CLINIC ASSOCIATION

3100 EUCLID AVENUE KANSAS CITY, MISSOURI

A Well Equipped Institution for the Nervous and Mental Diseases and Alcohol Drug and Tobacco Addictions

Beautiful Location Large, Well Shaded Grounds Spacious Porches, All Modern Methods for Restoring Patients to a Normal Condition

Elderly People Accepted — Special Rates

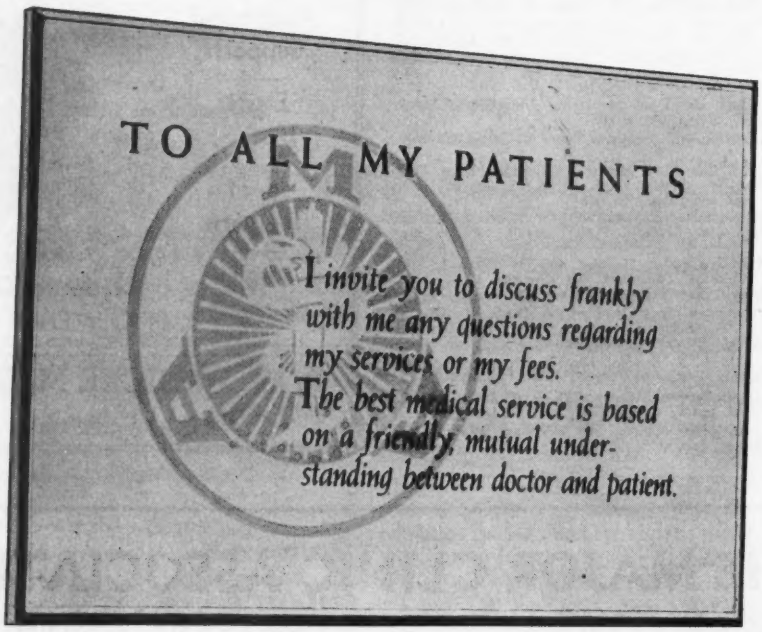
HERMON S. MAJOR, M.D.
Medical Director

HERMON S. MAJOR, JR.
Business Manager

announcing

A NEW PUBLIC RELATIONS AID

. . . to boost your PR rating


TO ALL MY PATIENTS
I invite you to discuss frankly with me any questions regarding my services or my fees.
The best medical service is based on a friendly, mutual understanding between doctor and patient.

NEW OFFICE PLAQUE

- ✓ **dark brown lettering on buff**
- ✓ **harmonizes with any office decor**
- ✓ **measures 11½ by 7¾ inches**
- ✓ **for desk or wall**
- ✓ **laminated plastic finish**

As you know, a physician's best public relations is carried on right in his own office. Here the physician gets acquainted with his patients . . . gives them a chance to talk over problems . . . builds a feeling of mutual understanding between patient and doctor.

Your American Medical Association has designed an attractive new office plaque to be displayed prominently on an office desk or wall. This is a graphic invitation to patients to talk over professional services and fees. Patients like to ask questions, but often are hesitant to do so. This plaque will open the door to better relations with your patients. Order one today.

PRICE
$1
POSTPAID

Order Department
AMERICAN MEDICAL ASSOCIATION
535 North Dearborn Street
Chicago 10, Illinois

Cook County Graduate School of Medicine
ANNOUNCES CONTINUOUS COURSES

SURGERY—Intensive Course in Surgical Technic, Two Weeks, starting March 3, March 17, March 31.
Surgical Technic, Surgical Anatomy & Clinical Surgery, Four Weeks, starting March 3, June 2.
Surgical Anatomy & Clinical Surgery, Two Weeks, starting March 17, June 16.
Surgery of Colon & Rectum, One Week, starting March 3, April 7.
Personal Course in General Surgery, Two Weeks, starting April 14.
Gallbladder Surgery, Ten Hours, starting April 21.
Basic Principles in General Surgery, Two Weeks, starting March 31.
Breast & Thyroid Surgery, One Week, starting June 23.
Esophageal Surgery, One Week, starting June 23.
Thoracic Surgery, One Week, starting June 2.
Fractures & Traumatic Surgery, Two Weeks, starting June 16.
GYNECOLOGY—Intensive Course, Two Weeks, starting March 17, April 21.
Vaginal Approach to Pelvic Surgery, One Week, starting March 31, May 5.
OBSTETRICS—Intensive Course, Two Weeks, starting March 31, June 2.
PEDIATRICS—Intensive Course, Two Weeks, starting April 7.
Informal Clinical Course, every two weeks.
Cerebral Palsy, Two Weeks, starting July 7.
MEDICINE — Intensive General Course, Two Weeks, starting May 5.
Electrocardiography & Heart Disease, Two Weeks, starting March 17.
Gastroenterology, Two Weeks, starting May 19.
Hematology, One Week, starting June 16.
Gastroscopy & Gastroenterology, One Week Advanced Course, starting June 23.
UROLOGY — Intensive Course, Two Weeks, starting April 28.
Ten Day Practical Course in Cystoscopy starting March 17, March 31, April 14.
DERMATOLOGY—Intensive Course, Two Weeks, starting May 5.

TEACHING FACULTY—ATTENDING STAFF OF COOK COUNTY HOSPITAL
Address: Registrar, 707 South Wood St., Chicago 12, Ill.

Medical and Surgical Supplies for Doctors of Medicine and Hospitals.

Munns Medical Supply Co.
512 Kansas Ave.
Topeka, Kansas

THE BROWN SCHOOL

Four distinct units. Tiny Tots through the Teens. Ranch for older boys. Special attention given to educational and emotional difficulties. Speech, Music, Arts and Crafts. A staff of 12 teachers. Full time Psychologist. Under the daily supervision of a Certified Psychiatrist. Registered Nurses. Private swimming pool, fireproof building. View book. Approved by State Division of Special Education.

BERT P. BROWN, DIRECTOR
PAUL L. WHITE, M.D., F.A.P.A.,
MEDICAL DIRECTOR
P. O. Box 4008, Austin, Texas

THE
MEDICAL PROTECTIVE
COMPANY
FORT WAYNE, INDIANA

PROFESSIONAL PROTECTION
EXCLUSIVELY
SINCE 1899

specialized service
assures "know-how"

TOPEKA Office:
J. E. McCurdy, Rep.,
1035 Randolph Avenue,
Telephone 2-3027

Rapid strides have been and are being made in the development of emergency medical call systems, the Council on Medical Service of the A.M.A. reported recently. Approximately 80 per cent of the country's large medical societies have such plans, 364 having been in operation at the end of 1951. Counties with few residents and few physicians may effectively rely on the normal physician-patient relationships in emergencies.

Rx Zemmer

PHARMACEUTICALS

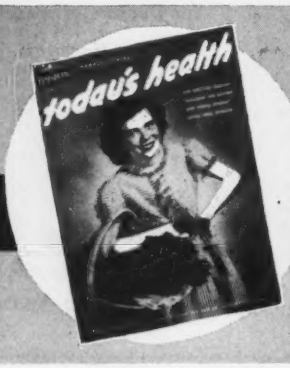
A complete line of laboratory controlled ethical pharmaceuticals. Chemists to the Medical Profession since 1903. KA-3-52

THE ZEMMER COMPANY, Pittsburgh 13, Pennsylvania

AMERICA'S AUTHENTIC HEALTH MAGAZINE

today's health

AMERICAN MEDICAL ASSOCIATION



BUILDS FAITH IN YOU AND YOUR WORK

IN YOUR WAITING ROOM

3 YEARS $6.50 2 YEARS $5.00

1 YEAR $3.00

THE UNIVERSITY OF KANSAS SCHOOL OF MEDICINE

Announces Postgraduate Courses In

OPHTHALMOLOGY AND OTOLARYNGOLOGY
March 17, 18, 19, 20 & 21, 1952

Guest Instructors:

ALSTON CALLAHAN, M.D., Professor of Ophthalmology and Chairman of Department, University of Alabama Medical College, Birmingham.
LOUIS H. CLERF, M.D., Professor of Laryngology and Broncho-Esophagology, Jefferson Medical College, Philadelphia.
FRANCIS E. LE JEUNE, M.D., Professor of Otolaryngology and Head of Department, Tulane University of Louisiana School of Medicine, New Orleans.
ALFRED E. MAUMENEE, M.D., Professor of Ophthalmology and Chairman of Department, Stanford University School of Medicine, San Francisco.
VICTOR H. MOORMAN, M.D., Otolaryngologist, Grace and St. Elizabeth's Hospitals, Hutchinson, Kans.
WINFRED L. POST, M.D., Otolaryngologist, Freeman Hospital, Joplin, Mo.
HAROLD G. SCHEIE, M.D., Associate Professor of Ophthalmology, University of Pennsylvania & Hospital, Philadelphia.
HAROLD F. SCHUKNECHT, M.D., Assistant Professor of Otolaryngology, University of Chicago Medical School, Chicago.
ROBERT B. WILSON, M.D., Otolaryngologist, Kansas City, Kans.

ANESTHESIOLOGY
April 14, 15 & 16, 1952

Guest Instructors:

R. M. S. BARRETT, M.D., Anesthesiologist, St. Louis.
WESLEY BOURNE, M.D., Professor Emeritus of Anesthesiology, McGill University, Montreal, Canada.
RALPH T. KNIGHT, M.D., Clinical Professor of Anesthesiology, University of Minnesota Medical School, Minneapolis.
LUCIEN E. MORRIS, M.D., Associate Professor of Anesthesiology, University of Iowa College of Medicine, Iowa City.
A. E. OSTERBERG, Ph.D., Department of Medicine, Abbott Laboratories, North Chicago, Ill.
THOMAS H. SELDON, M.D., Associate Professor of Anesthesiology, Mayo Foundation Graduate School of Medicine, University of Minnesota; Director, Division of Anesthesiology, Mayo Clinic, Rochester.
ROBERT W. VIRTUE, Ph.D., Assistant Professor of Anesthesiology, University of Colorado School of Medicine, Denver.

GERIATRICS
March 24, 25 & 26, 1952

Guest Instructors:

LEONARD J. GOLDWATER, M.D., Sc.D., Professor of Industrial Hygiene, Columbia University College of Physicians and Surgeons, New York City.
JULIUS JENSEN, M.D., Pd.D., Associate Professor of Clinical Medicine, Washington University School of Medicine, St. Louis.
WILLIAM K. ISHMAEL, M.D., Assistant Professor of Medicine, University of Oklahoma School of Medicine, Oklahoma City.
THOMAS H. McGAVACK, M.D., Professor of Clinical Medicine, New York Medical College, New York City.
ROBERT M. PERLMAN, M.D., Institute of Endocrinology and Gerontology, San Francisco.
MALFORD W. THEWLIS, M.D., The Thewlis Clinic, Wakefield, R. I.

Subjects to be Discussed:

Degenerative Arthritis.
Geriatrics—General Considerations.
Degenerative Diseases of Bone in the Aging.
Old Syphilis.
The Cholesterol Problem.
The Trend of Endocrine Gland Changes in Aging Individuals.
Common Accidents Occurring in Elderly Diabetics in Relation to Coma and Surgery.
Rehabilitation of Markedly Debilitated Aged and Aging Subjects.
Occupational Potentialities of the Cardiac Patient.
Hormones and the Aging Heart.
A Study of 175 "Cardiacs" Without Heart Disease.

CLASSIFIED ADVERTISEMENTS

WANTED—Doctor, young or old, general practice. Write the Journal 1-52.

WANTED—Young Kansas Draft exempt active general practitioner who has had sufficient training to do all minor and emergency surgery to permanently locate. City and surrounding industrial population 1,000—closest opposition 30 miles. This location is open as a result of the young physician recently being called to service who grossed $12,000 per year. A hospital district surrounding this city has been permanently organized and a new modern eight-bed hospital will be constructed here in the near future. Write the Journal 2-52.

FOR SALE—Will sacrifice. Entire office equipment. Town of 8,000 in southern Kansas location. Two good hospitals. Reason for selling, retiring. Write the Journal 3-52.

Merck & Mallinckrodt ® Reagents
KLINE TEST ANTIGEN (LAMOTTE)
PYREX LABORATORY GLASS WARE
PIPETTES AND BURETTES
PRECISION EQUIPMENT
HARTMAN-LEDDON SPECIALTIES
LABORATORY SUPPLIES & EQUIPMENT
KANSAS OWNED
Southwest Scientific Corporation
122 S. St. Francis Wichita 2, Kansas

TROWBRIDGE TRAINING SCHOOL
Established 1917

For unusual children. Medical and psychiatric supervision. Experienced teachers. Individual special training. Home atmosphere. Enrollment limited. Approved and registered by the Council of Medical Education and Hospitals of the A.M.A. Pamphlet.

E. H. TROWBRIDGE, SR., M.D.
1905 BRYANT BUILDING KANSAS CITY 6, MO.

Nationally advertised Surgical Supplies and Equipment have been placed at Topeka, Joplin, Kansas City and St. Joseph for your convenience by—

GOETZE NIEMER CO.

Management by Dr. W. F. Goetze, a member of the American Medical Association, assures intelligent servicing of your orders.

THE LATTIMORE-FINK LABORATORIES
Topeka El Dorado
Kansas

J. L. Lattimore, A.B., M.D., Pathologist
A. A. Fink, A.B., M.D., Pathologist
H. C. Ebendorf, M.T. Serologist
A. C. Keith, B.S., Chemist
L. W. Hull, A.B., Bacteriologist
Walter Norris, A.B., Chemist

Anatomical and Clinical Pathology

Containers Furnished Upon Request

ACCIDENT • HOSPITAL • SICKNESS
INSURANCE
FOR PHYSICIANS, SURGEONS, DENTISTS EXCLUSIVELY

ALL PREMIUMS COME FROM PHYSICIANS SURGEONS DENTISTS ALL CLAIMS GO TO

$5,000 accidental death	$8.00
$25.00 weekly indemnity, accident and sickness	Quarterly
$10,000.00 accidental death	$16.00
$50.00 weekly indemnity, accident and sickness	Quarterly
$15,000.00 accidental death	$24.00
$75.00 weekly indemnity, accident and sickness	Quarterly
$20,000.00 accidental death	$32.00
$100.00 weekly indemnity, accident and sickness	Quarterly

COST HAS NEVER EXCEEDED AMOUNTS SHOWN. ALSO HOSPITAL POLICIES FOR MEMBERS' WIVES AND CHILDREN AT SMALL ADDITIONAL COST

85c out of each $1.00 gross income used for members' benefits

$4,000,000.00 Invested Assets
$18,300,000.00 Paid for Claims
$200,000.00 deposited with State of Nebraska for protection of our members
Disability need not be incurred in line of duty—benefits from the beginning day of disability

PHYSICIANS CASUALTY ASSOCIATION
PHYSICIANS HEALTH ASSOCIATION
50 Years under the same management
400 FIRST NATIONAL BANK BLDG., OMAHA 2, NEBRASKA

Therapy for Vascular Headache to Reverse the Physiologic Disturbance

Headache, a problem encountered in all kinds of medical practice, may occur in association with any of a variety of disorders, some organic, other purely functional.

Among the several types, functional headaches present the greatest problem because of their obscure etiology and recurrent nature.

Among these are:

Migraine (both classical and variant forms)
Tension headache
Psychogenic headache
Histaminic cephalgia

Wolff and his co-workers established that the pain of these headches is due to disturbance of the tonus of cranial blood vessels — hence the term *vascular headaches.*

The craniovascular changes associated with the several phases of the typical migraine attack are:

Vasoconstriction — to which the visual prodromata are attributable. It is possible to abort the attack during this phase in all but a few cases. (See treatment below.)

Vasodilatation — as the vessels lose their tone, exaggerated pulsations set in, resulting in the throbbing pain which characterizes vascular headache. Treatment for the attack is still effective during this phase. (See below.)

Vessel Edema — if the vasodilation continues for too long, vessel walls become edematous; this changes the character of the pain to a steady, intense aching. The attack can now no longer be checked, even with maximum dosage of specific drugs. *Moreover, sustained headache often induces reflex neck muscle tension, a source of residual pain.*

Therapy: 1. Reduce the frequency of attacks — psychotherapy and regulation of living habits to avoid fatigue and nervous tension.

2. Relieve the acute attack — of the numerous drugs which have been tried, ergotamine and its derivative preparations have proved most effective. The newest product is oral tablets of Cafergot®, N. N. R. (ergotamine with caffeine 'Sandoz'). When dosage is adjusted to the needs of the individual, Cafergot will give good relief in 85% of cases. It enables a greater number of patients to benefit from early administration since the oral route simplifies treatment as compared to parenteral therapy.

The dosage procedure is:

1. Take 2 tablets at first sign of the attack.
2. If attack continues, take one additional tablet every ½ hour until attack is terminated *(max. 6 tabs. per attack).*

Many migraine patients delay taking medication until the attack is at its height. Explicit dosage instructions may be forgotten unless the patient comes to realize their importance. Therefore, to encourage adherence to correct procedure, we have prepared pads outlining detailed dosage instructions. Supplies of these INSTRUCTION SLIPS will gladly be sent upon request.

GENERAL REFERENCES: DeJong, R.: Chicago M. Soc. Bull 54: 106, 1951. Friedman, A.: Modern Headache Therapy, St. Louis, C. V. Mosby Co., 1951. Wolff, H.: Headache and Other Head Pain, N. Y., Oxford Univ. Press, 1948.

Sandoz Pharmaceuticals
DIVISION OF SANDOZ CHEMICAL WORKS, INC.
68 CHARLTON STREET, NEW YORK 14, N. Y.

Index to Advertisers

Abbott Laboratories XIV
American Meat Institute..... XII
Ayerst, McKenna and Harrison, Ltd. 153
Brown School 161
Continental Casualty Company..... XVIII
Cook County Graduate School of Medicine..... 161
Duncan Laboratories 151
Florida Citrus Commission..... 155
General Electric Company, X-ray Department. XVII
Goetze Niemer Company..... 163
Hanicke, P. W., Manufacturing Company..... 159
Kansas Oxygen Division..... 157
Lattimore-Fink Laboratories 163
Lederle Laboratories 149
Lilly, Eli, and Company ..... Facing XVIII
Major Clinic 159
Mead Johnson and Company..... Back cover
Medical Protective Company..... 161
Merck and Company, Inc. V
Munns Medical Supply Company, Inc. 161
Neurological Hospital Association 164
Parke, Davis and Company, Inc.....
..... Inside front cover and III
Pfizer, Charles, and Company, Inc..... X and XI
Philip Morris and Company..... 147
Physicians Casualty Association..... 163
Ralph Sanitarium XVI
Reynolds, R. J., Tobacco Company..... XIII
Sandoz Pharmaceuticals 164
Schering Corporation XV
Searle, G. D., and Company..... 141
Smith-Dorsey Company .....Inside back cover
Southwest Scientific Corporation..... 163
Squibb, E. R., and Sons..... VI and VII
Trowbridge Training School 163
University of Kansas Medical Center..... 162
Upjohn Company 143
Winthrop-Stearns, Inc. 145
Woodcroft Hospital 157
Wyeth, Inc. IX
Zemmer Company 162

The Neurological Hospital, 2625 West Paseo, Kansas City, Missouri, a voluntary hospital providing the care and treatment of nervous and mental patients, and associate conditions.

H.P.S. *Sixty*

60% Protein

. . . . yet as delicious as any milk beverage

A mixture of milk protein concentrate, soy protein, whole egg powder, powdered sugar, and flavoring, H. P. S. Sixty provides

Protein.....60%
Fat.....1.5%
Carbohydrate.....27%

...tanding
...ins are
...le taste

...102 cal-

... (6 oz.
...(three 6
...ed with
...in; with

...t be in-
...n can be
...epatitis,
...on, and
...aise the

H.
su
a

...ION

DATE DUE

Stormont Medical Library,
State House,
Topeka, Kansas.

In infant formulas...

proper

caloric

distribution

calls for

adequate added carbohydrate

FREQUENT mention in authoritative pediatric literature supports the classic caloric distribution of 15% protein, 35% fat and 50% carbohydrate for infant formulas.

This assures ample protein for development of sound tissue structure. And it supplies *adequate carbohydrate* to spare protein for its essential functions, meet energy needs, promote good fat metabolism and maintain water balance.

This classic caloric distribution is conveniently represented by 1 part evaporated milk and 2 parts water with 5 per cent added carbohydrate—roughly 1 tablespoon of Dextri-Maltose to each 5 ounces of formula.

For over 40 years, milk and Dextri-Maltose formulas with these approximate proportions have enjoyed consistent clinical success.

MEAD'S

MEAD JOHNSON & CO.
EVANSVILLE 21, IND., U. S. A.